CLINICAL AND COST CONSEQUENCES OF NON-ADHERENCE IN THE END-STAGE RENAL DISEASE POPULATION

by

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Dedication

In the memory of my wonderful grandparents who taught me how to love, listen, respect, and be kind to all forms of life in the world.

To my husband, Anwell, a true philosopher who teaches me to embrace new concepts, broadens my intellectual spectrum, awakens my inner creativity, endures my outrageous thoughts, moves me with so many romantic innovations, and loves me unconditionally the way I am.

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Abstract

Results from this study indicate that non-adherence in hemodialysis sessions marginally affects health care costs and does not significantly increase the likelihood of kidney transplantation failure.

This dissertation explores the short-term and long-term impacts of non-adherence in hemodialysis (HD) sessions on health care costs and on kidney transplantation failure. This dissertation uses a conventional non-adherence measure, a broader data set which includes HD patients nationwide, and rigorous statistical models to tackle these research questions. Informed policy recommendations are especially important because of the difficulty for dialysis patients to adhere to treatments.

There are five principal findings from my first dissertation paper, which investigates the impact of non-adherence on separately billable (SB) Medicare Allowable Payments (MAP), one of the two components that constitute the dialysis costs for HD patients. There is a negative association between non-adherence and SB MAP, consistent across three different regression estimations, namely, ordinary-least square (OLS), two-stage least square (2SLS), and log-linear regression models. Since SB MAP have a skewed distribution, the estimation from the OLS model could be biased and inefficient. The instrumental variables, the distance from patient residence to dialysis facilities and its square term, are weak instruments because the partial R-square is very small. The standard error from the 2SLS is quite large, suggesting the instability of the estimation.

A log-linear model was applied to reduce skewness, but the estimates need to be retransformed back on the unlogged scale, which could lead to biases if heteroscedasticity is present on the log scale. Finally, results from three lagged effect models do not support the hypothesis that dialysis patients who are non-adherent in the concurrent period would use more SB drug injectables in the following periods.

My second dissertation paper explores the association between non-adherence and composite rate (CR) costs, the second component of dialysis costs, for dialysis facilities. There are four principle findings. CR costs, similar to SB MAP, represent a skewed distribution. Hence, a log transformation of CR costs might be a better measure for the dependent variable. The explanatory power increases significantly for log-linear models comparing to that for OLS models. There is no association between non-adherence and CR costs except for the log-linear model without facility control variables. Finally, adding facility control variables significantly increases the explanatory power for log-linear models. This effect is not as pronounced for OLS models.

My third dissertation paper explores whether non-adherence is a contributing factor to kidney transplantation failure. The results from the Cox proportional hazards models consistently show that non-adherence in hemodialysis sessions does not have a significant influence on kidney transplantation failure after controlling for none, some, or a full list of patient characteristics. The coefficient estimates from a binary non-adherence measure also confirm this finding.

Findings from this dissertation may provide valuable information for dialysis patients, dialysis facilities, and policy makers when faced with concerns related to non-adherence.

Chapter I

Chapter I. Introduction

Medical expenditures associated with treating dialysis patients have rapidly increased, accounting for 6.4% of the Medicare budget with 506,256 prevalent patients, according to the U.S. Renal Data System in 2007. There is little literature pertaining to the economic consequences of non-adherence for ESRD patients.

To fill this void, I examined the short-run economic consequences and long-run health deterioration outcome of non-adherence. Informed policy recommendations are especially important because of the difficulty for dialysis patients to adhere to three treatments per week and take medication 6 to 10 times per day (Loghman-Adham, 2003).

For my first paper, I investigate the causality between non-adherence and health care costs, and explore whether the fluctuation in health care costs due to non-adherence would continue or stabilize in subsequent periods. Most previous studies use a relatively small number of study observations, representing only a subset of Medicare HD patients. This study uses the population of 416,164 Medicare HD patients, substantially increasing the statistical power. Earlier studies used cross-sectional data to conduct statistical analyses, failing to control for plausible time trends. This study uses longitudinal data from 2004 to 2006 and controls for time fixed effects. Finally, previous studies do not handle the potential *endogeneity*, when the independent variable of interest is correlated

with the error term due to either simultaneity or omitted variable bias. This study tackles this concern by applying a two-stage least square (2SLS) estimation.

I define non-adherence as the number of dialysis sessions skipped by a dialysis patient in a month. The measure of health care costs is separately billable (SB) Medicare Allowable Payments (MAP). I hypothesize that non-adherence would lead to a significant drop in SB MAP, and am interested in investigating the magnitude of this short-run impact. In addition, I would like to test the hypothesis that non-adherent patients would adjust for missed treatments by using more drug injectables to reach their clinical target level in the subsequent period immediately following the non-adherent month, and that this lagged impact would vanish over a longer period of time.

I shift the focus of study population from dialysis patients to dialysis facilities in my second paper. This paper investigates whether there is an association between non-adherence, as measured by the average HD sessions missed per patient per month, and composite rate (CR) costs for dialysis facilities, using a nationally representative sample. Results from this study might be useful for both dialysis facilities and the CMS. From the dialysis facilities' perspective, they could implement strategies to increase the adherence rate if the results show that they are faced with revenue loss with no meaningful cost-savings due to non-adherence. From the CMS's perspective, it is important to know what the magnitude of non-adherence on CR costs is, in order to better monitor reimbursement and regulate budgetary issues.

Policy mandates often target facilities directly, not patients. Since a fully-bundled ESRD payment system was implemented in January 1, 2011, relevancy for issues explored by this paper increases. CMS may want to explore the importance of non-

adherence and determine whether a pay-for-performance scheme to reward facilities with higher adherence rates should be implemented.

Previous literature does demonstrate the relation between non-adherence and kidney transplantation failure, showing that non-adherence with use of immunosuppressive drugs is a major cause of graft loss. (Garcia *et al.*, 1997; Michelon *et al.*, 1999; Morrissey *et al.*, 2005). However, many of these studies were limited by focusing on only one medical institution, failing to control for other exogenous variables, and neglecting the impact of non-adherence before a transplantation occurs. My third paper uses Medicare data that include hemodialysis patients who receive kidney transplantation nationwide. I use Cox Proportional Hazards models to predict kidney transplantation failure controlling for a full list of patient case-mix characteristics, and conduct sensitivity analysis using a nonlinear non-adherence measure.

My study results provide a different perspective in addressing the effect of non-adherence on kidney transplantation failure. Previous studies established the association between non-adherence in medication, which occurs after the kidney transplantation is operated, and kidney transplantation failure. The non-adherence measure the researchers used was immunosuppressive drugs, not dialysis sessions. I examine the impact of non-adherence even before the kidney transplantation takes place. If non-adherence in hemodialysis sessions is associated with a higher kidney transplantation failure rate, If there is an association between non-adherence in hemodialysis sessions and kidney transplantation failure, then this finding could possibly affect the kidney allocation score system, or be used to target patients for counseling about adherence prior to transplant

and for more aggressive monitoring after transplant. I use a subset of Medicare HD patients, the kidney transplantation recipients, to evaluate this impact.

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Chapter II

Chapter II. The Intertemporal Impact of Non-adherence on Separately Billable Medicare Allowable Payments in Medicare Hemodialysis Patients

Abstract

Objective. To understand whether a causal relationship exists between non-adherence and health care costs in the concurrent period and to explore whether this impact extends to the following periods for Medicare hemodialysis (HD) patients.

Data Sources. CMS Form 2728 and Medicare claims from 2004-2006.

Study Design. I use a two-stage least square (2SLS) model to investigate the impact of non-adherence on health care costs. Non-adherence is measured by the number of dialysis sessions an HD patient skipped in each month. Health care costs are measured by Medicare Allowable Payments (MAP) for separately billable (SB) services, including Erythropoietin (EPO), iron, vitamin D, other injectables, and certain laboratory services. The estimates from this model are compared with the estimates from the ordinary least squares (OLS) and log-linear models. Additionally, three lagged effect models are fitted to see whether the fluctuation in SB MAP due to non-adherence stabilized after one, two, or three months.

Principal Findings. The OLS model provides more reliable results with a tighter standard error distribution in examining the association of non-adherence on SB MAP,

after comparing coefficient estimates derived from OLS, 2SLS, and log-linear models**.** The findings obtained through the OLS model suggested that dialysis facilities would lose $67.65 in payment if a patient skipped one treatment, which was lower than the average SB MAP per treatment of $86.52. Since the impact of non-adherence on SB MAP is significant, though small, the finding could potentially provide a financial incentive for dialysis facilities to monitor and improve patient adherence. Results from the lagged effect models supported the hypothesis that non-adherent patients would make up for missed treatments by using slightly more drug injectables to reach their clinical target level in subsequent periods.

Conclusions. Medical costs and patient outcomes are two components used to evaluate the effect of non-adherence on treatment efficiency. As long as the saved cost of missed treatments offsets the cost of increased morbidity, non-adherence could potentially have cost saving effects for the CMS. Future research should focus on measuring the cost of increased morbidity due to non-adherence in order to fully examine the net cost effect.

Key Words. Hemodialysis, non-adherence, health care costs, instrumental variables, ESRD

Introduction

The causal relationship between non-adherence and the use of injectable medications and laboratory tests associated with dialysis treatments has not been well established. Elevating costs in treating dialysis patients has drawn much attention in the end-stage

renal disease (ESRD) community from policy makers, health care researchers, dialysis providers, and dialysis patients. Using an OLS approach, I found that there is a negative association between non-adherence and SB MAP, controlling for a comprehensive list of patient and facility characteristics. The coefficient estimates on non-adherence differ substantially amongst the OLS, 2SLS, and log-linear regression models. There is a modest statistically significant association between lagged months non-adherence measures and the current month SB MAP.

On average, dialysis patients need to take medication six to ten times per day (Loghman-Adham, 2003). In-center hemodialysis patients need to undergo dialysis sessions three times a week, each session taking about three to four hours. They often watch television or take a nap during their sessions. It takes an enormous amount of discipline for dialysis patients to adhere to routine sessions and properly take the prescribed medications. Based on different definitions of non-adherence, prevalence has been reported to vary from as little as 2 percent to as much as 100 percent (Leggat, 2005). To date, few studies have investigated the association between non-adherence and ESRD health care costs. Of these, most use a relatively small number of study observations, which makes generalizability questionable. Most studies use cross-sectional data to conduct analysis, failing to control for plausible time trends that may be associated with health care costs. None of these studies deal with the concern of *endogeneity,* when the independent variable of interest − non-adherence − is correlated with the error term due to either simultaneity or omitted variable bias. Causality between non-adherence and health care costs cannot be drawn. All these issues have prompted the need to conduct a more rigorous study in examining the economic consequences of non-adherence.

The total ESRD expenditures for Medicare dialysis patients increased from 5.5 billion dollars in 1991 to 20.4 billion dollars in 2006, which represents a 73% increase. The prevalent ESRD patients increased from roughly 60,000 in 1980 to 500,000 in 2006, representing an 84% increase. The results of this study suggest that non-adherence in hemodialysis sessions should not be encouraged, even when considering cost-savings for the CMS. Rather point to how significant, in terms of dollars, non-adherence can be.

Literature Review

Previous literature already demonstrates that non-adherence would lead to worsening health outcomes, e.g., higher mortality, and worsening quality of life. This chapter fills the void in the literature by providing more concrete information to explore the impact of non-adherence on health care costs, as measured by SB MAP.

Within the ESRD-related literature, issues concerning patient non-adherence with hemodialysis (HD) prescriptions have been discussed extensively. A large body of research regarding predictors and clinical outcomes of non-adherence has been published in the clinical literature (Denhaerynck et al., 2005; Jarzembowski et al., 2004; Leggat et al., 1998; Leggat et al., 2005; Saran et al., 2003). Most researchers define non-adherence in dialysis patients when there is an interdialytic weight gain >1.5 kg, a serum phosphorus level >6 mg/dL, and/or a predialysis serum potassium level >5.5 mEq/L, or when dialysis sessions are shortened or skipped by the patient. Many studies found a positive correlation between non-adherence in dialysis sessions and worsening health outcomes, and a negative association between non-adherence and quality of life

(Denhaerynck et al., 2005; Leggat et al., 1998; Saran et al., 2003). Nevertheless, it is surprising to find that the economic consequences of non-adherence have rarely been investigated in the ESRD community. Only a few studies have applied cost-effectiveness or cost-utility analyses to estimate the economic impact of non-adherence in renal transplant patients. For example, Swanson and colleagues (1992) estimated that the non-adherence related additional hospital cost, after transplantation, amounts to $900 per non-adherent patient per year. Cleemput and colleagues (2004) conducted cost-utility analyses to assess non-adherence and its economic consequences in a renal transplant population and found that non-adherent recipients' lifetime treatment costs are actually lower due to lower life expectancies.

It is important to understand whether non-adherence has a significant impact on dialysis costs facing the current cost-consciousness U.S. healthcare environment. In 1973, the Medicare ESRD Program was established as a national health insurance program for people diagnosed with end-stage renal disease. Over the past few decades, the total number of prevalent dialysis patients and the total expenditure of the ESRD program have continuously increased. In 2007, there were 506,256 prevalent patients in the U.S. The medical expenditures associated with treating these patients have reached $20 billion, accounting for 6.4% of the Medicare budget (U.S. Renal Data System [USRDS] 2007). The improved mortality rates of prevalent ESRD patients and the continuing growth of incident ESRD patients both contribute to the rising cost pressures encountered by the Centers for Medicare and Medicaid Services.

Non-adherence is commonly observed in dialysis patients (Curtin et al., 1999; Leggat et al., 1998). Although dialysis is lifesaving, it only replaces 10% of normal renal

function. Patients may continue to encounter many medical problems such as salt and water retention, hyperparathyroidism, hypertension, and heart disease, among others (Loghman-Adham, 2003). On average, dialysis patients need to take medication 6 to 10 times per day (Loghman-Adham, 2003). It takes a tremendous amount of discipline and determination for patients to adhere to routine sessions and properly take the prescribed medications. The non-adherence issue is particularly important for those living in the United States. Bleyer and colleagues' (1999) studies on international comparisons of patient adherence on hemodialysis found that roughly 2.3% of dialysis sessions were skipped by patients in the United States, whereas missed dialysis treatments were virtually nonexistent in Japan and Sweden.

There are wide variations in terms of what constitutes non-adherence. How researchers define their non-adherence measures would affect the estimated prevalence of non-adherence and associated mortality risks (Kimmel et al., 1998; Kimmel et al., 1995; Leggat et al., 1998; Saran et al., 2003). Based on these definitions, the prevalence of non-adherence has been reported to vary from as little as 2% to as much as 100% (Leggat, 2005). Because different definitions have been used, it is difficult to make direct comparisons across studies. Results of predictors of non-adherence are mixed. Most studies show that predictors of non-adherence in adult HD patients include age, race, sex, marital status, socioeconomic status, and educational level (Bame et al., 1993; Brownbridge et al., 1994; Gordon et al., 2003; Hoover, 1989; Morduchowicz et al., 1993). However, Leggat and colleagues (1998) did not find sex or education level statistically significant.

Most studies examining the issues regarding skipped and shortened HD sessions focus on patient characteristics and individual reasons leading to non-adherence (Gordon et al., 2003; Loghman-Adham, 2003). In general, younger patients, incident patients, low-income patients, African-Americans, and males are more likely to be associated with non-adherent behaviors. Reasons may include medical problems, life tasks, and difficulty in transportation. Conclusions drawn from these studies often emphasize the development of interventions to target patient-specific characteristics in order to improve the adherence of HD sessions. In terms of outcomes research, studies by Leggat and colleagues (1998), Loghman-Adham (2003), and Saran and colleagues (2003) have shown that non-adherence with HD treatment is associated with increased mortality risk. Missed or shortened dialysis sessions can reduce dialysis adequacy, a potential factor for increased mortality. A majority of dialysis patients suffer from anemia problems related to erythropoietin (EPO) deficiency and require renal anemia management. It has been shown that untreated or under-treated anemia in the dialysis population is associated with increased morbidity and mortality (Tong et al., 2001).

Summarizing non-adherence studies within the ESRD transplantation literature, Denhaerynck and colleagues (2005) concluded that non-adherence in adult renal transplant patients is associated with poor clinical outcomes. However, non-adherence results in lower life-time costs because of shorter survival as well as lower quality adjusted life years. Consistent determinants were age, social isolation, health beliefs, and health cognitions. Jarzembowski and colleagues (2004) examined pediatric patients who received renal transplantation and found that African-American recipients had a significantly higher rate of graft loss when compared to Caucasian and Hispanic

recipients. They drew the conclusion that non-adherence is a problem of great importance in the African-American pediatric transplant population. In contrast to the excellent long-term survival rate in pediatric receipts of renal transplantation, Ettenger and colleagues (2005) found that the long-term transplant outcomes in adolescents were disappointing because of non-adherence with immunosuppressive medications. With early identification and appropriate interventions, significant improvement in adolescent graft survival is highly possible.

There are several studies that investigated the impact of non-adherence with medication regimens on health care costs (Coambs et al., 1995; Sullivan et al., 1990). Cleemput and colleagues (2002) provided a literature review on the economics of non-adherence of therapeutic treatments and concluded that non-adherence is often associated with increased morbidity and mortality for chronic patients. Studies from Iskedjian and colleagues (1998), Sullivan and colleagues (1990), and Coambs and colleagues (1995) have all suggested positive correlations between non-adherence in medication and hospitalization admissions. Though it is very difficult to compare study results because of the lack of a gold standard in the assessment of methodology, the literature seems to support the premise that it is more costly to treat non-adherent patients than adherent ones. Clearly, the underlying core concept of these studies is based on the idea that higher adherence is desirable.

Non-adherence in medication utilization and refill behavior associated with cost pressure within Medicare, Medicaid, and VA population has also received considerable attention. Hirth and colleagues (2008) examined the relationship between out-of-pocket spending and cost-related medication underuse of hemodialysis patients across twelve

countries, and concluded that drug costs were associated with national drug financing policies as well as the non-adherence rate. Using data on diabetic management, Piette and colleagues (2004) found that VA enrollees, who generally have more generous drug coverage, reported less cost-related medication underuse than patients with no health insurance, patients with Medicare or Medicaid coverage, and even patients with private health insurance. Their study results also suggest that many diabetic patients use less than the required medication and have poorer health, due to cost-related non-adherence. Mojtabai and colleagues (2003) tested the association of prescription drug coverage with adherence to chronic disease medications and the association of cost-related poor adherence with health outcomes among Medicare beneficiaries at various income and out-of-pocket spending levels. Results showed a positive correlation between lack of drug coverage and cost-related poor adherence. Cost-related poor adherence is related to adverse health outcomes, lower income level, and higher out-of-pocket spending.

Hypotheses

I am interested in investigating the causal and intertemporal effects of non-adherence on SB MAP per month, using OLS, 2SLS, and log-linear models.

I would like to test the following two hypotheses: (1) An HD patient who is non-adherent in the current month will cause a lower SB MAP in that month due to a drop in the use of drug injectables and related services. (2) An HD patient who is non-adherent in the current month will increase the use in drug injectables in the following months, in order to make up for his missed treatments.

Conceptual Framework

My conceptual framework considers the non-adherence choice of a utility-maximizing HD patient. The patient faces the decision of how to spend his time in order to maximize his utility. In this case, the utility is a measure of the satisfaction derived from the allocation of time used to receive dialysis treatments or do other activities. To maximize his utility function, the patient must choose whether to adhere to routine dialysis treatments for the value of health benefits or to be non-adherent so that he can spend the time on other activities, which provide more utility. From the health perspective, receiving dialysis treatments affects the patient's utility directly because he should feel better after each treatment. The tradeoff is the opportunity costs for the three to four hour session which he could use to do other activities that might provide more utility for that patient. A rational patient should be less likely to skip routine sessions for long-term health benefits. A myopic patient may care more about short-term benefits (e.g., watching a movie, spending time with friends) rather than the long-term benefits (e.g., prolonged life expectancy).

Some patients who need to travel for a long time to get to the facility may be more likely to skip more sessions than patients who live nearby the facility. Since previous literature did not find the association between medication utilization and travel distance, I claim that resource utilization of SB services has no correlation with the distance that a patient needs to travel to get to the facility. These factors motivate the rationale for using travel distance as an instrumental variable to tackle the endogeneity

concern, for that distance is correlated with missed treatments but uncorrelated with SB MAP.

I consider two conceptual models. In the first model, the hypothesis is that healthier patients tend to skip more sessions based on their own perception of health status. These healthier patients in general have lower resource utilization in SB services. Assuming the presence of omitted variable bias (unobservable patient health status), the OLS estimate on non-adherence would tend to be biased away from the null. The rationale is that for patients who skip routine sessions, they would use fewer SB services, and thus the coefficient estimate on non-adherence would be negative. If I was able to observe the coefficient on this omitted variable of health status in which a healthier patient is characterized with more skipped sessions and uses fewer SB services, then the coefficient on this variable should be negative as well. Therefore, I expect to see a negative coefficient estimate on non-adherence, with a coefficient estimate from the 2SLS to be smaller than that from the OLS estimate, in absolute value.

In the second model, the hypothesis is that seriously ill patients tend to skip more because they are too fragile to go to the facility and receive treatments thrice a week. Since these patients demand more resource utilization on SB services, the coefficient estimate on the omitted health status measure should be positive. As stated before, the coefficient estimate of non-adherence on SB MAP should be negative. If the omitted variable bias exists, then the OLS estimate on non-adherence would be biased towards the null. Under this scenario, I expect to see the 2SLS coefficient estimate to be larger than that from the OLS estimate in absolute value.

Methods and Data

Methods

The OLS and log-linear models were first used to estimate the association between non-adherence and SB MAP, controlling for patient case-mix and certain facility characteristics. This was followed by the application of a 2SLS model using the distance from patient residence to dialysis facility, the square of distance, and the square root of distance as three instruments to tackle the potential endogeneity that lies between skipped sessions and SB MAP. Additionally, three lagged effect models were fitted to see whether the fluctuation in SB MAP due to non-adherence stabilizes after one, two, or three months. All regression analyses were weighted by the number of HD-equivalent sessions.

2.1 OLS estimation

Models of resource use for separately billable services could be estimated as either linear models or logarithmic models. Typically, health care cost data feature a skewed distribution in which a relatively small fraction of individuals account for a disproportionate fraction of costs. Logarithmic models are useful with skewed data. I examined both linear and logarithmic forms of the non-adherence case-mix models. For these analyses, the dependent variable was SB MAP per month ($SBMAP_{it}$) in the linear models and the log transformation of SB MAP per month ($\log(SBMAP_{it})$) in the

logarithmic models. The independent variable of interest, non-adherence (NA_{it}), and other exogenous variables were the same in both models.

Equation 2-1 specifies the OLS model, and Equation 2-2 specifies the log-linear model. The notations on *i* and *t* refer to patient *i* admitted month *t* for dialysis treatments.

Equation 2-1 $$SBMAP_{it} = \alpha_0 + \alpha_1 NA_{it} + \alpha_2 FAC_{it} + \alpha_3 X_{it} + \mu_i + \nu_t + \varepsilon_{it}$$

Equation 2-2 $$\log(SBMAP_{it}) = \pi_0 + \pi_1 NA_{it} + \pi_2 FAC_{it} + \pi_3 X_{it} + \mu_i + \nu_t + \omega_{it}$$

NA_{it} is the non-adherence measure that represents the number of dialysis sessions a HD patient skipped in each month. FAC_{it} is a vector of facility characteristics, including a dummy variable indicating a dialysis facility's status (hospital-based or freestanding (reference group)), facility size (< 5,000 treatments, 5,000-9,999 treatments, > 10,000 treatments (reference group)), chain status (large dialysis organization, regional chain, unknown chain status, and independent chain as the reference group), and metropolitan status. X_{it} is a set of patient demographics including age, sex, race, time since renal replacement therapy, body surface area, BMI<18.5 kg/m^2, clinical hematocrit value, and 37 comorbid conditions. The census region ***(*** μ_i ***)*** and year (ν_t) dummies are also included to control for regional fixed effects and time trends. Finally, I used robust standard errors to account for the heteroscedasticity in error terms.

2.2 2SLS estimation

If unmeasured variables (e.g. patient's health status) affecting SB MAP are also correlated with non-adherence, results of the OLS estimation are likely to be biased. To ensure consistent estimates of the non-adherence measure, I re-estimated this association by using instrumental variables. The instrumental variables I used were the distance from a patient's residence to the dialysis facility, the square of distance, and the square root of distance. This set of distance instruments have been used extensively in various publications (McClellan et. al, 1994; Hirth et. al, 2003). A good set of instruments should fulfill the criterion in which they are strongly correlated with the endogenous variable but uncorrelated with the dependent variable.

For the first stage estimation (Equation 2-3), I regressed non-adherence on distance, distance^2, distance$^{0.5}$, patient characteristics, facility characteristics, and census region and year dummies to obtain the predicted probabilities of non-adherence. Then, I regressed SB MAP on predicted probabilities of non-adherence as well as all other exogenous variables as the second stage estimation (Equation 2-4). I performed a Durbin-Wu-Hausman test to check for the existence of endogeneity.

Equation 2-3

$$NA_{it} = \beta_0 + \beta_1 DIST_{it} + \beta_2 DIST^2 + \beta_3 DIST^{0.5} + \beta_4 FAC_{it} + \beta_5 X_{it} + \mu_i + \nu_t + e_{it}$$

Equation 2-4 $$SBMAP_{it} = \gamma_0 + \gamma_1 \hat{NA} + \gamma_2 FAC_{it} + \gamma_3 X_{it} + \mu_i + \nu_t + \eta_{it}$$

2.3 Lagged effect models

I fitted three lagged effect models to see whether non-adherence in the prior month (Equation 2-5), prior two months (Equation 2-6), and prior three months (Equation 2-7) has an influence on the current month SB MAP. Similar to previous estimations, I controlled for the same set of exogenous variables, census regions and time fixed effects.

Equation 2-5 $$SBMAP_{it} = \phi_0 + \phi_1 NA_{i,t-1} + \phi_2 FAC_{it} + \phi_3 X_{it} + \mu_i + \nu_t + \tau_{it}$$

Equation 2-6 $$SBMAP_{it} = \theta_0 + \theta_1 NA_{i,t-2} + \theta_2 FAC_{it} + \theta_3 X_{it} + \mu_i + \nu_t + \sigma_{it}$$

Equation 2-7 $$SBMAP_{it} = \lambda_0 + \lambda_1 NA_{i,t-3} + \lambda_2 FAC_{it} + \lambda_3 X_{it} + \mu_i + \nu_t + \rho_{it}$$

Data

Data for the measures of SB MAP, patient characteristics, and factors associated with the interrupted dialysis month were obtained from the ESRD Medical Evidence Report (CMS Form 2728) and/or Medicare claims. The sources of facility characteristics were obtained from the Medicare Independent Renal Dialysis Facility Cost Reports (Form CMS 265-94) and the Medicare Hospital Cost Reports (Form CMS 2552-96).

Originally, there were 8.9 million patient-month-facility records for 2004-2006 in the crude data set. Since I am merely interested in Medicare in-center HD patients, I excluded dialysis patients whose primary modality is either peritoneal dialysis or home hemodialysis. The reason that I only investigated in-center HD patients is because 90 percent of dialysis patients use this modality, and the payment schemes for three modality types are different. This procedure excluded 568,316 records (6.4 percent). I used the

standard outer fence method[1] to exclude influential SB MAP observations, so that the resulting models would characterize the pattern that represented most HD patients, rather than being disproportionately affected by a few exceptional, non-representative, and perhaps erroneous cases. This eliminated 102,104 records (1.2 percent). I then excluded observations with dialysis sessions greater than 20 sessions per month, because it is unlikely for an HD patient to receive more than 20 dialysis treatments in a month. This eliminated 6,326 records (0.1 percent). I excluded any distance measure that was greater than 150 miles. This cutoff threshold is based on a consultation with a clinical nephrologist. This eliminated another 261,824 records (3.2 percent). Subsequently, I excluded any missing values from any covariates used in this study, which eliminated 538,680 records (6.8 percent). Finally, I incorporated the information about rural and urban status from another data source. After excluding the missing values generated from this procedure, I obtained 7,188,698 patient-month-facility records, which accounts for 80.8 percent of the original 8.9 million data file (Table 2-1).

Measures

Dependent variables

Since the data set does not include actual costs of SB services, MAP were used as a proxy to measure resource use, calculated from payment data on the claims. In this analysis,

[1] Upper outer fence: 75th percentile + 3×interquartile range (IQR, the 75th percentile – the 25th percentile)
Lower outer fence: 25th percentile - 3×interquartile range (IQR, the 75th percentile – the 25th percentile)

MAP for the top injectables were adjusted according to the reimbursement levels during the first quarter of 2006, since the CMS recently changed its reimbursement levels to reflect the typical facility acquisition costs.

SB services included EPO, iron, vitamin D, other injectables, laboratory services that were either (1) billed by dialysis facilities or (2) billed by freestanding laboratory suppliers and ordered by physicians who received Medicare capitation payments for treating ESRD patients, and other services that were billed by dialysis facilities (i.e., syringes and other supplies) provided by dialysis facilities and their affiliates to individuals receiving chronic dialysis under Medicare's ESRD payment system. MAP for SB services were obtained from 2004-2006 Medicare claims files for all HD patients with Medicare as the primary payer. A log transformation of SB MAP is used as a second dependent variable.

Independent variable of interest

The non-adherence measure − the number of HD sessions skipped − was derived using the following strategy. Medicare claims from 2004 to 2006 were selected for analysis only if the number of dialysis sessions was between 0 and 20 for each claim. The average number of HD equivalent dialysis sessions was 12 sessions. Several events may explain low sessions in HD sessions, including starting month for dialysis with or without hospitalization, withdrawal from the dialysis services, transplant with or without hospitalization, death with or without hospitalization, hospitalization only, switching dialysis modality, transfer between facilities, and training sessions. Multiple events

based on these aforementioned categories were identified using the patient-month-facility level data set.

The measure of skipped sessions was then defined as fewer than 12 HD equivalent sessions billed, with none of the above events identified on each record. If the record is identified as a skipped month, I then calculated the total number of skipped sessions for that month, using 12 minus dialysis sessions received for that month. For example, suppose a dialysis patient was identified as a skipped patient in December 2004. If that patient-month-facility record shows that he received eight HD sessions in that month, then the total number of HD sessions skipped in December is four sessions.

Other studies have used different measures for non-adherence. The most common four measures for non-adherence are skipped HD sessions, shortened HD sessions by 10 or more minutes, an interdialytic weight gain of more than 5.7 percent or dry weight, or a serum phosphate of greater than 7.5 mg/Dl (Leggat et. al, 1998). Since my data set did not include information besides the number of HD sessions skipped, it is important to understand whether this measure is a sensitive proxy to capture the non-adherence measure in general. Based on a study from Leggat and colleagues (1998), researchers showed that there was a high degree of correlation among various definitions of non-adherence. For example, if a patient is classified as non-adherent using one definition, e.g., an interdialytic weight gain of more than 5.7 percent, then the odds of this patient being identified as a non-adherent patient using other definitions (e.g., skipped sessions) are significantly higher. The strongest correlation was between skipping and shortening HD sessions.

Instrumental variables

There are three instrumental variables used in this study. I used the Great Circle Distance formula (Distance = 3959 $\times$arcos(sin(latitude of facility zipcode/57.3) $\times$sin(latitude of patient zipcode/57.3) + cos(latitude of facility zipcode/57.3) $\times$cos(latitude of patient zipcode /57.3) $\times$cos((longitude of facility zipcode – longitude of patient zipcode)/57.3)) to calculate the distance between patient residence zip code centroid and dialysis facility's zip code. In addition, the square and square root terms of the distance measure are used as two other instruments to test for nonlinearity.

Patient characteristics

Several patient characteristics including demographics (age, sex, race), time since start of renal replacement therapy (RRT), body surface area, an indicator of low body mass index (BMI<18.5 kg/m^2), functional statuses, and clinical comorbidities that have significant impacts on explaining the variation of SB MAP based on prior research (Hirth et al., 2003; Hirth et al., 2007), were included in the regression models as control variables. Data for the measures of patient characteristics were obtained from the ESRD Medical Evidence Report (CMS Form 2728) and/or Medicare claims. Clinical comorbidities were obtained from CMS Form 2728 and/or Medicare claims, since there were issues concerning underreporting of comorbidities using only CMS Form 2728. Additionally, this Medical Evidence Report does not capture changes in patients' comorbidities after the initiation of RRT. Comorbid conditions based purely on this form were not perfectly

measured. Clinical comorbidity conditions were based on diagnosis codes reported on Medicare inpatient, outpatient, skilled nursing facility, home health, hospice, and physician claims covering a specified period of time.

These claims-based comorbidity measures were limited to recent diagnoses (i.e., during the previous six months only) for acute conditions such as gastrointestinal bleeding. Longer periods were used for chronic conditions. Several "look back" periods (i.e., diagnoses in last year vs. last two years) were tested to determine their ability to predict costs. The most predictive look back period was chosen as the measure of the comorbidity to be entered into the regression models.

Facility characteristics

The relationship between non-adherence and the SB MAP may be affected by the inclusion or exclusion of facility characteristics. Therefore, several facility characteristics including hospital-based vs. freestanding, facility size, membership in major chains, and urban vs. rural location, metropolitan status, and census region were also used in the regression models.

Results

Descriptive analysis

To test the normality assumption for statistical models, I compared the shape for the distribution of SB MAP and log (SB MAP). Figure 2-1 shows that SB MAP has a right skewed distribution. After a log transformation on SB MAP, the new distribution looked more like a bell-shape, although there seems to be a tail that was marginally skewed to the left (Figure 2-2).

There are a total of 439,181 patient-month-facility records with at least one skipped HD session (Figure 2-3). The average number of skipped sessions amongst these patients is 2.34. Out of these records, 35.6 percent contains one skipped session and 19.9 percent shows three skipped sessions in the month.

The summary statistics of all variables are listed in Table 2-2. The mean SB MAP per patient per month is $1,049.6 (SD = $759.24). The average log (SB MAP) is 6.68 (SD = 0.85). On average, the number of HD sessions skipped for a HD patient in a month is 0.05 (SD = 0.21). The average travel distance from patient residence to the dialysis facility is 7.31 miles (SD = 11.74 miles).

For patient demographics, the majority of HD patients in this study are between 45 and 79 years old, male, and White. In terms of other patient characteristics and comorbid measures, the mean body surface area using the Dubois Formula ($BSA(m^2) = 0.20247 \times Height(m)^{0.725} \times Weight(kg)^{0.425}$) per 0.1 m^2 is 1.87 (SD = 0.25). Four percent of these patients were underweight (body mass index < 18.5 kg/m^2). About 49 percent of these patients have been on renal replacement therapy for more than 3 years. The most commonly observed comorbidities are diabetes (60 percent), ischemic heart disease (51 percent), peripheral vascular disease (45 percent), and cardiac dysrhythmia (34 percent). The least observed comorbidity is esophageal varices (0.04

percent). With respect to facility characteristics, 93 percent of these patients are from free-standing facilities, 66 percent are from dialysis facilities which provide more than 10,000 dialysis treatments, 70 percent are from large dialysis organization (Fresenius, Gambro, Davita, Renal Care Group, Dialysis Centers Inc, and National Nephrology Associates), 18 percent are from rural locations, and 83 percent are from metropolitan areas.

Using a simple strategy to test the validity of the instrumental variable, the distance measure, I assigned distance into five groups: 0–2 miles, 2–5 miles, 5–10 miles, 10–15 miles, and >15 miles (Table 2-2). A good instrument should be correlated with the independent variable of interest and uncorrelated with the dependent variable. From this table, I observed that as distance gets larger, the number of skipped sessions increases accordingly, though the magnitude of this increase is moderate. This finding suggests that there is a modest correlation between the instrumental variable (distance) and the independent variable of interest (non-adherence). Furthermore, it shows that SB MAP remain consistently stable across the five distance groups. More encouragingly, the mean values for the four most commonly observed comorbidities do not change at the five distance group measures. These two phenomena suggest that there is no correlation between the instrumental variable (distance) and the dependent variable (SB MAP), and between the instrumental variable (distance) and the exogenous variables (four comorbidities).

Regression analysis

To formally test for the strength of the instrumental variable, I conducted several specification tests. The F-statistic from the first-stage least square regression is 179.59, which is higher than 10, the cutoff threshold suggested by Staiger and Stock (1995). However, the partial R-square is 0.01%, which is very small. Combining these two results, I conclude that the distance measure is a weak instrument for non-adherence.

I use distance (per 10 miles), its square, and its square root as three instrumental variables in my first-stage estimation. The logic for including the square and square root terms of distance is to check for the effect of nonlinearity. The result shows that if distance increases by 10 miles, the number of skipped sessions would decrease by 0.0026, statistically significant at the 99 percent confidence interval. The sign of this direction is not as expected, and the magnitude is again small. The coefficient estimates on $distance^2$ and $distance^{0.5}$ suggest that as distance gets larger, the speed of the increase in the number of skipped sessions slightly goes up. The results are statistically significant at the 99 percent significant level.

The comparison of the OLS and 2SLS regression results can be found in Table 2-5. Model 1 and Model 2 provide a comparison between OLS and 2SLS results using SB MAP per month as the dependent variable. Model 3 and Model 4 use a different dependent variable, log (SB MAP). All models controlled for census region and time fixed effects.

In Model 1, the OLS estimate on non-adherence shows that if an HD patient skipped one HD session in the month, his SB MAP for the month would drop by $67.65 (SE = $1.29). This result is statistically significant at the 99 percent confidence level. The 2SLS estimate of non-adherence (Model 2) shows that if one HD patient skipped a

session in the month, his SB MAP for that month would decrease by $2343.29 (SE = $179.19), statistically significant at the 95 percent confidence level.

For models with the log transformed SB MAP, the OLS estimate of non-adherence (Model 3) is -0.095 (SE = 0.001), statistically significant at the 99 percent confidence level. After taking the exponentiation of the coefficient estimate, i.e., exp (-0.095), I derived the multiplier of non-adherence on SBMAP, which is 0.91. The interpretation is that if an HD patient skipped one HD session, his SB MAP for that month would drop by 9 percent, which on the dollar scale is equal to $94.46 ($1049.6×0.09=$94.46).

Model 4 shows the 2SLS estimate of non-adherence on log (SB MAP). The coefficient estimate is -7.60 (SE = 0.37), statistically significant at the 99 percent confidence level. The multiplier for non-adherence is 0.0005, suggesting that if one HD patient skipped one session in the month, his SB MAP for that month would decrease by 99.95%, or in dollar scale, $1049.08.

When comparing the explanatory power between the OLS and 2SLS estimations using SB MAP as the dependent variable, I found the R-square is higher in the OLS estimation (Model 1: R^2 = 7.47%; Model 2: R^2 = 5.30%). This finding holds when using the log (SB MAP) as the dependent variable (Model 3: R^2 = 6.18%; Model 4: R^2 = 1.37%). In general, the explanatory power of log-linear models was slightly lower than that of linear models.

Finally, the OLS results for the three lagged effect models are presented in Table 2-6. The coefficient estimate of one-month lagged non-adherence on the current month SB MAP is $18.01 (SE = $1.32), suggesting that if an HD patient skipped a session in the

prior month, the current month SB MAP would increase by $18.01. Similarly, the two month lagged model shows that if an HD patient skipped one session two months ago, the current month SB MAP would increase by $18.91 (SE = $1.36). The three-month lagged model shows that the current month SB MAP would increase by $19.41 (SD=1.40) if an HD patient skipped one treatment three months ago. All results are statistically significant at the 99 percent confidence level.

Sensitivity analysis

It is highly likely to observe more voluntary withdrawal cases for dialysis patients who are close to the end of life. Based on my identification strategy for non-adherence, I was not able to distinguish whether individual missed treatments were due to permanent withdrawal or temporary withdrawal. To address this possible misclassification concern, I conducted a sensitivity analysis in which I dropped observations on the month of death and the month prior to death, to ensure the results are not biased.

After excluding the observations of "month of death" and "month prior to death," the sample size was reduced from 7,188,698 to 6,969,739 records (Table 2-7). For the OLS model using SB MAP as the dependent variable, the coefficient estimate on non-adherence changed modestly from -67.65 to -68.58, and remained statistically significant. For the 2SLS model, the coefficient estimate changed from -2343.29 to -2254.71. The coefficient estimates on other covariates changed on a moderate scale, as compared with the original model. The coefficient estimate on non-adherence for the OLS model using log SB MAP/month as the dependent variable is -0.096 (multiplier=0.91), which remains

the same as the original model. That for the 2SLS model is -7.41 (multiplier=0.0006), which is pretty similar to the one derived from the original 2SLS model. For the three lagged effect models, Table 2-8 shows that the coefficient estimates on non-adherence remain small and do not differ much from the original models.

Since low income patients may have a higher tendency of skipping dialysis sessions, I added county-level income information from the Area Resource File, and re-examined the impact of non-adherence on the SB MAP to understand the importance of adding income information in the estimation. The results showed that the effect of adding income information is so trivial that there is basically no change in coefficient estimates on non-adherence and no improvement in explanatory power. The downside from adding the income information is a loss in statistical power because 556,341 records were excluded due to missing values. I did not report the coefficient estimates here. The full set of estimated coefficients is available from the author upon request.

Discussion

With the use of Medicare data, which includes all Medicare HD patients, I was able to obtain a representative study population, and increase the statistical power and generalizability from this study. This study uses three modeling approaches, OLS, 2SLS, and log-linear regression models, to estimate the impact of non-adherence on SB MAP and compares the strength and weakness of each model. After comparing coefficient estimates derived from OLS, 2SLS, and log-linear models, I conclude that the OLS model provides more reliable results with a tighter standard error distribution in

examining the association of non-adherence on SB MAP. Based on the specification test results, distance is a weak instrument. This property could likely explain the extremely large and implausible 2SLS estimates. Future work could be conducted to find a better instrument in order to tackle the endogeneity concern. A log-linear model may better satisfy the normality assumption of statistical models, but the explanatory power is lower than that from the OLS.

The findings obtained through the OLS model suggested that dialysis facilities would lose $67.65 in payment if a patient skipped one treatment, which was lower than the average SB MAP per treatment of $86.52. Since the impact of non-adherence on SB MAP is significant, though small, the finding could potentially provide a financial incentive for dialysis facilities to monitor and improve patient adherence. Results from the lagged effect models supported the hypothesis that non-adherent patients would make up for missed treatments by using slightly more drug injectables to reach their clinical target level in subsequent periods. Overall, the study results suggest that non-adherence in HD sessions causes a decrease in SB MAP for facilities, and generates SB cost-savings for the CMS. The size of savings is moderate.

Because the 2SLS estimate on non-adherence is greater than the OLS estimate, the findings support the second conceptual model − sicker patients tend to skip more. If the CMS and dialysis facilities would like to improve the patient adherence rate, it would be more efficient to target this sicker population and provide incentives to address its concerns.

Since the CMS implemented a full bundling system on January 1, 2011, which pays a fixed amount per patient per treatment in order to reimburse both composite rate

costs and separately billable items, it is important to understand how this new bundling system will change implications of skipped treatments for dialysis facilities and the CMS. Based on study results which show that skipping sessions is associated with lower SB utilization, with some evidence of slightly more SB utilization in the following months to make up for the missed treatments, it is expected that dialysis facilities would respond to non-adherence because they earn more profit margins when patients maintain scheduled sessions and need not use more SB resources for following months. Facilities can design appointment follow-up programs to target those patients who commonly skip HD treatments. From the CMS perspective, since the bundled payment is made per patient per treatment, there is enough financial incentive for facilities to improve patient adherence because they will not receive reimbursement from a missed session. The CMS probably needs not design policy intervention in improving patient adherence at this point.

Medical costs and patient outcomes are two components used to evaluate the effect of non-adherence on treatment efficiency. Non-adherence could potentially be cost saving for the CMS as long as the saved cost of missed treatments offsets the cost of increased morbidity. Future research should focus on measuring the cost of increased morbidity due to non-adherence in order to fully examine the net cost effect.

It is important to note one limitation. Non-adherence, as defined in this study, is measured conservatively. For instance, if a patient is identified to have an event (e.g., hospitalization) in a month, then he will not be defined as a "skipped" patient for that month based on my identification strategy. In reality, he might be both "hospitalized" and "non-adherent" for that month. For months with 31 days, patients may receive 13

treatments instead of 12 treatments. Suppose a record shows that a patient received 11 treatments in a 31-day month, without any other event being identified. Using my identification strategy, this patient would be reported as skipping one treatment, although in reality he skipped two treatments. To the extent that this non-adherence measure was underestimated, the prevalence of non-adherence should be greater than 0.05 sessions per month, and the coefficient estimates on non-adherence as well as other covariates could also be affected.

Figure 2-1. Distribution of SB MAP/month

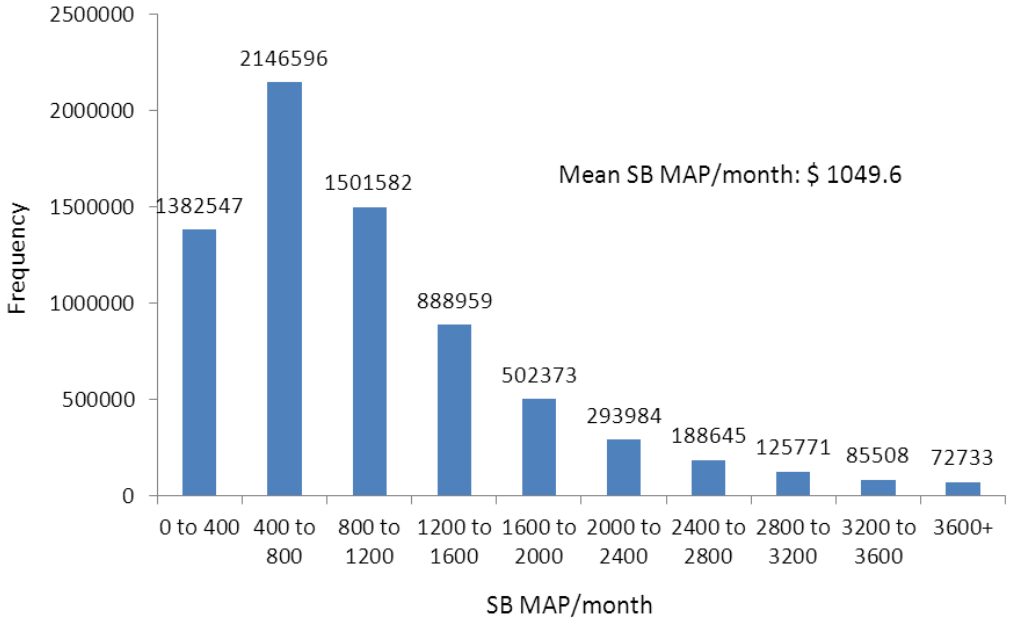

Figure 2-2. Distribution of log (SB MAP/month)

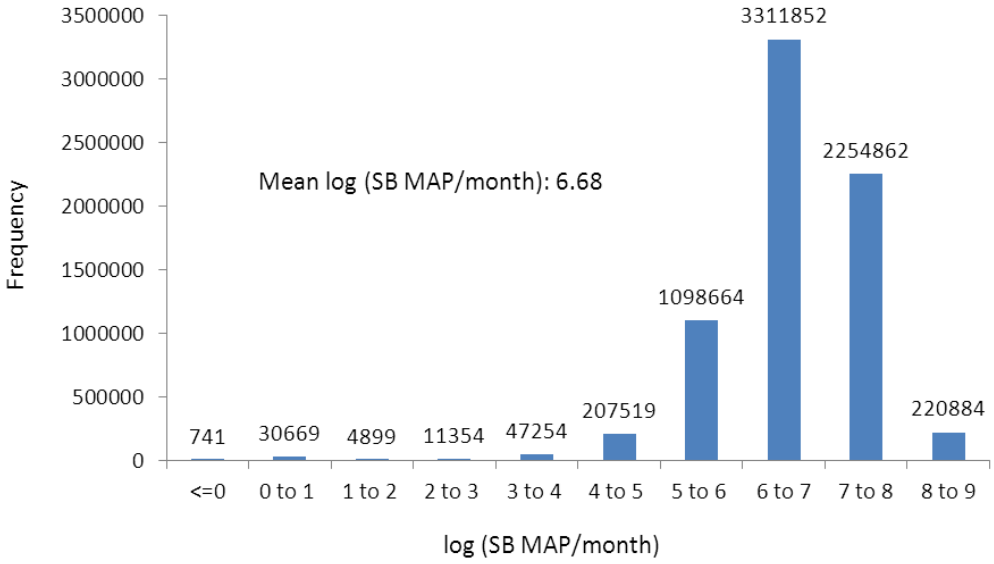

Figure 2-3. Distribution of skipped sessions for the 439,181 pat-mon-fac records with at least one skipped HD session

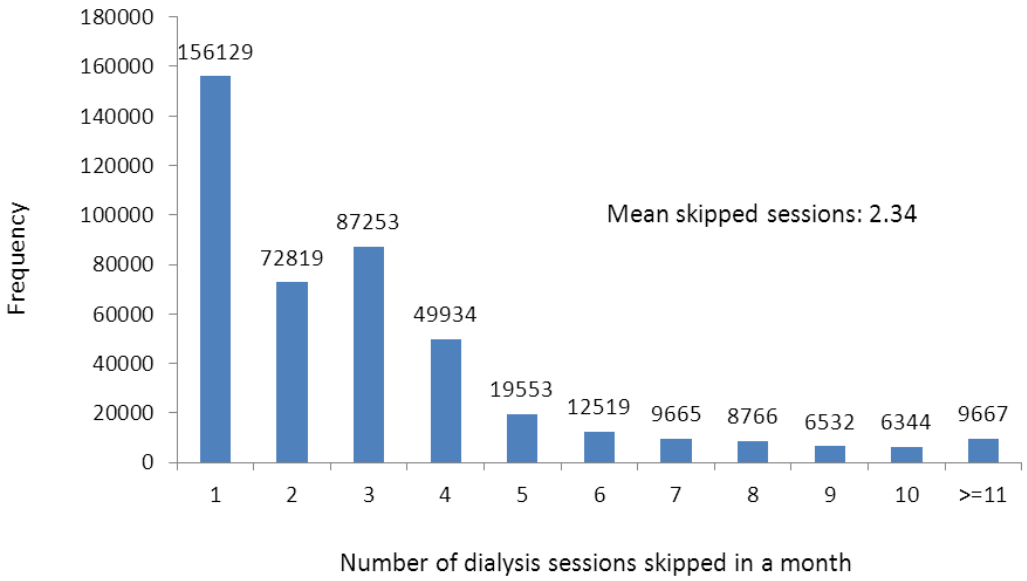

Table 2-1. The derivation of final sample size, 2004-2006

Steps	Procedures	N	Unit
1	Original 2004-2006 records	8,899,748	pat-mon-fac
2	Limit to Medicare HD patients only	8,331,432	pat-mon-fac
3	Exclude influential SB MAP/month observations using outer fence definition*	8,229,328	pat-mon-fac
4	Exclude observations with dialysis sessions > 20 sessions per month	8,223,002	pat-mon-fac
5	Exclude distance to facility > 150 miles (suggested by a nephrologist)	7,961,178	pat-mon-fac
6	Exclude missing values from any covariates	7,422,498	pat-mon-fac
7	Add rural/urban variable from another data source	7,188,698	pat-mon-fac

*Outer fence definition:

-Upper outer fence: 75th percentile + 3*interquartile range (IQR, the 75th percentile-the 25th percentile)=1344.95+3*(1344.95-457.89)=4006.12

-Lower outer fence: 25th percentile - 3*interquartile range (IQR, the 75th percentile-the 25th percentile)=457.89-3*(1344.95-457.89)=-2203.29

Table 2-2. Summary statistics of all variables, 2004-2006

Variables	Mean	S.D.
Dependent variables		
SB MAP per month	1049.60	759.24
log (SB MAP per month)	6.68	0.85
Other variable		
SB MAP per session	86.52	63.98
Variable of interest		
Number of HD sessions skipped in the month	0.05	0.21
Instrumental variable		
Distance from patient residence to facility (in miles)	7.31	11.74
Demographic variables		
Ages <18 yrs	0.0009	-
Ages 18-44 yrs	0.13	-
Ages 45-59 yrs	0.26	-
Ages 60-69 yrs	0.23	-
Ages 70-79 yrs	0.24	-
Ages 80+ yrs	0.13	-
Female	0.47	-
Race: Native American	0.02	-
Race: Asian	0.03	-
Race: Black	0.40	-
Race: White	0.54	-
Race: Other	0.01	-
Race: Unknown/missing	0.0002	-
Patient characteristics and comorbidities		
Body surface area (Dubois formula), per 0.1 m^2	1.87	0.25
Underweight (BMI <18.5 kg/m^2)	0.04	-
Started RRT during month	0.01	-
1 previous month of RRT	0.01	-
2 previous months of RRT	0.01	-
3 previous months of RRT	0.02	-
4 previous months of RRT	0.02	-
5 previous months of RRT	0.02	-
6 previous months of RRT	0.02	-
7 previous months of RRT	0.02	-
8 previous months of RRT	0.02	-
9 previous months of RRT	0.02	-
10-12 previous months of RRT	0.05	-
2nd year of RRT	0.16	-
3rd year of RRT	0.14	-
3 years or more of RRT	0.49	-
Inability to ambulate (2728)	0.03	-
Inability to transfer (2728)	0.01	-
Smoking	0.03	-
Alcohol Dependence between 1999-2004	0.05	-
Drug Dependence between 1999-2004	0.04	-
Cardiac Arrest within one year	0.01	-
Cardiac dysrhythmia within one year	0.34	-

Ischemic heart disease within one year	0.51	-
Pericarditis within one year	0.01	-
Cerebrovascular disease within one year	0.26	-
Diabetes within one year	0.60	-
Peripheral vascular disease within one year	0.45	-
Chronic obstructive pulmonary disease within one year	0.28	-
Acquired immunodeficiency disease within one year	0.02	-
Human immnodeficiency virus within one year	0.01	-
Bacterial Pneumonia six months ago	0.005	-
Hepatitis B within one year	0.01	-
Other Hepatitis between 1999-2004	0.07	-
Opportunistic Infection six months ago	0.001	-
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.002	-
Septicemia within six months	0.04	-
Gastro-Intestinal (GI) Tract Bleeding six months ago	0.004	-
GI Ulcer - no hemorrhage within six months	0.01	-
Esophogeal Varices within six months	0.0004	-
Acquired Hemolytic Anemias within one year	0.01	-
Hereditary Hemolytic Anemias between 1999-2004	0.02	-
Sickle-Cell Anemia between 1999-2004	0.004	-
Leukemia within one year	0.004	-
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.01	-
Lymphoma within two years	0.01	-
Metastatic Cancers within one year	0.01	-
Multiple Myeloma within one year	0.01	-
Breast, Prostate, Colorectal and Other Cancers within one year	0.08	-
Hyperparathyroidism within one year	0.10	-
Monoclonal Gammopathy within one year	0.01	-
Myelofibrosis within one year	0.005	-
Myelodysplastic Syndrome between 1999-2004	0.01	-
Facility characteristics		
Hospital-based facility	0.07	-
Facility size: < 5,000 treatments	0.08	-
Facility size: 5,000 - 9,999 treatments	0.26	-
Facility size: 10,000+ treatments	0.66	-
Large dialysis organization (chain1-chain6)	0.70	-
Regional chain	0.10	-
Independent	0.17	-
Unknown	0.03	-
Rural location	0.18	-
Metropolitan area	0.83	-
Micropolitan area	0.12	-
Not in micro or metro area	0.05	-
N(pat-mon-fac records)	7,188,698	

Table 2-3. Descriptive statistics of number of skipped sessions, SB MAP, and four comorbidities by five distance groups

Distance groups (miles)	*N (pat-mon-fac)*	*% Total*	Means					
			# skipped sessions	SB MAP	Diabetes	Ischemic heart disease	Peripheral vascular disease	Cardiac dysrhythmia
(1) 0 - 2	2,006,946	27.92%	0.045	1050.62	0.61	0.51	0.45	0.34
(2) 2 - 5	2,137,152	29.73%	0.048	1053.89	0.60	0.50	0.45	0.34
(3) 5 - 10	1,506,926	20.96%	0.047	1057.95	0.59	0.50	0.45	0.34
(4) 10 - 15	600,312	8.35%	0.047	1050.87	0.59	0.51	0.44	0.34
(5) 15+	937,362	13.04%	0.049	1021.64	0.61	0.50	0.43	0.33
Total	7,188,698							

Table 2-4. First-stage regression results to predict number of skipped sessions

Variables	Number of skipped sessions
Instrumental variables	
Distance (per 10 mile)	-0.0026**
	(0.00033)
Distance^2 (per 10 mile)	0.00015**
	(0.000022)
Distance square root (per 10 mile)	0.0066**
	(0.00047)
Census region fixed effects	yes
Time trends	yes
R^2	0.01%
Observations	7,188,698

Note: Standard errors are in parentheses.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

** Significantly different from zero at 99 percent confidence.

Table 2-5. OLS and 2SLS regression results

Variables	Dependent variable: SB MAP/month					
	OLS (1)			IV-2SLS (2)		
	Coeff.		S.E.	Coeff.		S.E.
Independent variable of interest						
Number of skipped sessions	-67.65	**	1.29	-2343.29	**	179.19
Demographic variables						
Ages <18 yrs	172.49	**	9.32	176.52	**	11.17
Ages 18-44 yrs	128.75	**	1.00	126.99	**	1.20
Ages 45-59 yrs	49.32	**	0.80	48.60	**	0.96
Ages 60-69 yrs (ref.)	ref.		-	-		-
Ages 70-79 yrs	-63.79	**	0.80	-63.67	**	0.96
Ages 80+ yrs	-111.00	**	0.98	-110.97	**	1.18
Female	101.14	**	0.61	101.19	**	0.73
Race: Native American	-38.13	**	2.29	-38.29	**	2.75
Race: Asian	18.59	**	1.58	18.57	**	1.89
Race: Black	98.15	**	0.63	96.82	**	0.76
Race: White or Unknown/missing (ref.)	ref.		-	-		-
Race: Other	8.82	**	2.68	8.27	**	3.21
Patient characteristics and Comorbidities						
Started RRT during month	-137.50	**	3.60	-135.37	**	4.31
1 previous month of RRT	392.64	**	2.29	391.45	**	2.74
2 previous months of RRT	336.00	**	2.28	334.66	**	2.73
3 previous months of RRT	177.55	**	2.04	175.65	**	2.45
4 previous months of RRT	60.40	**	2.09	58.49	**	2.50
5 previous months of RRT	8.63	**	2.08	6.69	**	2.49
6 previous months of RRT	-17.58	**	2.13	-19.55	**	2.56
7 previous months of RRT	-40.51	**	2.12	-42.50	**	2.54
8 previous months of RRT	-73.23	**	2.17	-75.24	**	2.60
9 previous months of RRT	-89.89	**	2.19	-91.83	**	2.63
10-12 previous months of RRT	-104.37	**	1.32	-106.44	**	1.58
2nd year of RRT	-90.04	**	0.79	-91.86	**	0.95
3rd year of RRT	-57.07	**	0.84	-58.35	**	1.00
3 years or more of RRT (ref.)	ref.		-	-		-
Body surface area (Dubois formula)	278.23	**	1.31	279.68	**	1.57
Underweight (BMI <18.5 kg/m^2)	26.63	**	1.44	26.29	**	1.72
Inability to ambulate (2728)	23.67	**	1.73	23.83	**	2.08
Smoking	-36.74	**	1.54	-38.16	**	1.85
Alcohol Dependence between 1999-2004	67.32	**	1.26	65.79	**	1.51
Drug Dependence between 1999-2004	58.73	**	1.40	57.84	**	1.67
Cardiac Arrest within one year	100.11	**	2.52	100.48	**	3.03
Cardiac dysrhythmia within one year	89.53	**	0.63	89.85	**	0.76
Ischemic heart disease within one year	48.32	**	0.63	48.55	**	0.75
Pericarditis within one year	148.62	**	2.68	148.87	**	3.21
Cerebrovascular disease within one year	26.86	**	0.66	27.13	**	0.80
Diabetes within one year	42.56	**	0.61	43.26	**	0.73
Peripheral vascular disease within one year	73.81	**	0.59	74.11	**	0.71
Chronic obstructive pulmonary disease within one year	73.44	**	0.64	73.41	**	0.77
Acquired immunodeficiency disease within one year	138.89	**	3.38	138.35	**	4.05
Human immnodeficiency virus within one year	97.74	**	3.84	97.19	**	4.60
Bacterial Pneumonia six months ago	35.66	**	4.50	36.01	**	5.40

Hepatitis B within one year	42.58	**	2.54	42.57	**	3.04
Other Hepatitis between 1999-2004	-37.89	**	1.11	-38.02	**	1.33
Opportunistic Infection six months ago	114.75	**	7.74	115.13	**	9.28
Pneumococcal pneumonia, emphysema, lung abcess within six months	36.40	**	6.50	36.71	**	7.80
Septicemia within six months	111.53	**	1.50	111.47	**	1.80
Gastro-Intestinal (GI) Tract Bleeding six months ago	155.54	**	4.71	155.51	**	5.65
GI Ulcer - no hemorrhage within six months	56.33	**	3.61	56.34	**	4.33
Esophogeal Varices within six months	339.89	**	13.50	340.16	**	16.17
Acquired Hemolytic Anemias within one year	52.15	**	2.42	52.65	**	2.90
Hereditary Hemolytic Anemias between 1999-2004	112.66	**	2.05	112.98	**	2.46
Sickle-Cell Anemia between 1999-2004	251.44	**	4.26	251.64	**	5.11
Leukemia within one year	130.66	**	4.18	130.86	**	5.01
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	91.96	**	2.56	91.97	**	3.07
Lymphoma within two years	91.23	**	3.33	91.33	**	4.00
Metastatic Cancers within one year	186.98	**	2.59	186.97	**	3.11
Multiple Myeloma within one year	299.74	**	3.08	299.93	**	3.69
Breast, Prostate, Colorectal and Other Cancers within one year	63.76	**	1.05	64.13	**	1.26
Hyperparathyroidism within one year	31.55	**	0.92	31.68	**	1.10
Monoclonal Gammopathy within one year	23.97	**	3.59	24.67	**	4.31
Myelofibrosis within one year	136.23	**	3.97	136.78	**	4.76
Myelodysplastic Syndrome between 1999-2004	267.45	**	2.55	267.73	**	3.05
Census region fixed effects			yes			
Time trends			yes			
R^2	7.47%			5.30%		
N (pat-mon-fac records)			7,188,698			

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

** Significantly different from zero at 99 percent confidence.

Table 2-5. OLS and 2SLS regression results (cont'd)

Variables	Dependent variable: log (SB MAP/month)							
	OLS (3)				IV-2SLS (4)			
	Coeff.	S.E.	Mult.		Coeff.	S.E.	Mult.	
Independent variable of interest								
Number of skipped sessions	-0.095	0.001	0.91	**	-7.60	0.37	0.0005	**
Demographic variables								
Ages <18 yrs	-0.045	0.011	0.96	**	-0.035	0.023	0.97	
Ages 18-44 yrs	0.089	0.001	1.09	**	0.087	0.002	1.09	**
Ages 45-59 yrs	0.023	0.001	1.02	**	0.023	0.002	1.02	**
Ages 60-69 yrs (ref.)	ref.	-	-		-	-	-	
Ages 70-79 yrs	-0.051	0.001	0.95	**	-0.051	0.002	0.95	**
Ages 80+ yrs	-0.093	0.001	0.91	**	-0.094	0.002	0.91	**
Female	0.12	0.001	1.13	**	0.12	0.002	1.13	**
Race: Native American	-0.026	0.003	0.97	**	-0.025	0.006	0.98	**
Race: Asian	0.041	0.002	1.04	**	0.040	0.004	1.04	**
Race: Black	0.13	0.001	1.14	**	0.13	0.002	1.14	**
Race: White or Unknown/missing (ref.)	ref.	-	-		-	-	-	
Race: Other	0.034	0.003	1.03	**	0.032	0.007	1.03	**
Patient characteristics and Comorbidities								
Started RRT during month	-0.21	0.004	0.81	**	-0.20	0.009	0.82	**
1 previous month of RRT	0.41	0.003	1.51	**	0.41	0.006	1.51	**
2 previous months of RRT	0.35	0.003	1.42	**	0.35	0.006	1.42	**
3 previous months of RRT	0.18	0.002	1.19	**	0.17	0.005	1.19	**
4 previous months of RRT	0.053	0.002	1.05	**	0.051	0.005	1.05	**
5 previous months of RRT	0.014	0.002	1.01	**	0.012	0.005	1.01	*
6 previous months of RRT	0.002	0.002	1.00		-0.0007	0.005	1.00	
7 previous months of RRT	-0.018	0.002	0.98	**	-0.02	0.005	0.98	**
8 previous months of RRT	-0.057	0.002	0.95	**	-0.059	0.005	0.94	**
9 previous months of RRT	-0.074	0.002	0.93	**	-0.077	0.005	0.93	**
10-12 previous months of RRT	-0.087	0.001	0.92	**	-0.090	0.003	0.91	**
2nd year of RRT	-0.075	0.001	0.93	**	-0.078	0.002	0.93	**
3rd year of RRT	-0.042	0.001	0.96	**	-0.043	0.002	0.96	**
3 years or more of RRT (ref.)	ref.	-	-		-	-	-	
Body surface area (Dubois formula)	0.26	0.001	1.30	**	0.27	0.0032	1.31	**
Underweight (BMI <18.5 kg/m^2)	0.012	0.002	1.01	**	0.012	0.0035	1.01	**
Inability to ambulate (2728)	0.016	0.002	1.02	**	0.017	0.0043	1.02	**
Smoking	-0.043	0.002	0.96	**	-0.045	0.0038	0.96	**
Alcohol Dependence between 1999-2004	0.070	0.001	1.07	**	0.067	0.0031	1.07	**
Drug Dependence between 1999-2004	0.056	0.002	1.06	**	0.055	0.0034	1.06	**
Cardiac Arrest within one year	0.074	0.003	1.08	**	0.075	0.0062	1.08	**
Cardiac dysrhythmia within one year	0.079	0.001	1.08	**	0.079	0.0016	1.08	**
Ischemic heart disease within one year	0.055	0.001	1.06	**	0.055	0.0015	1.06	**
Pericarditis within one year	0.13	0.003	1.13	**	0.13	0.0066	1.13	**
Cerebrovascular disease within one year	0.025	0.001	1.02	**	0.025	0.0016	1.03	**
Diabetes within one year	0.060	0.001	1.06	**	0.061	0.0015	1.06	**

Peripheral vascular disease within one year	0.065	0.001	1.07	**	0.065	0.0015	1.07	**
Chronic obstructive pulmonary disease within one year	0.066	0.001	1.07	**	0.066	0.0016	1.07	**
Acquired immunodeficiency disease within one year	0.125	0.004	1.13	**	0.12	0.0083	1.13	**
Human immnodeficiency virus within one year	0.080	0.004	1.08	**	0.079	0.0094	1.08	**
Bacterial Pneumonia six months ago	0.021	0.005	1.02	**	0.022	0.011	1.02	
Hepatitis B within one year	0.036	0.003	1.04	**	0.037	0.006	1.04	**
Other Hepatitis between 1999-2004	-0.051	0.001	0.95	**	-0.051	0.003	0.95	**
Opportunistic Infection six months ago	0.086	0.009	1.09	**	0.087	0.019	1.09	**
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.030	0.007	1.03	**	0.030	0.016	1.03	
Septicemia within six months	0.085	0.002	1.09	**	0.085	0.004	1.09	**
Gastro-Intestinal (GI) Tract Bleeding six months ago	0.12	0.005	1.13	**	0.120	0.012	1.13	**
GI Ulcer - no hemorrhage within six months	0.046	0.004	1.05	**	0.046	0.009	1.05	**
Esophogeal Varices within six months	0.27	0.015	1.31	**	0.27	0.033	1.31	**
Acquired Hemolytic Anemias within one year	0.006	0.003	1.01	*	0.008	0.006	1.01	
Hereditary Hemolytic Anemias between 1999-2004	0.089	0.002	1.09	**	0.090	0.005	1.09	**
Sickle-Cell Anemia between 1999-2004	0.17	0.005	1.18	**	0.170	0.010	1.18	**
Leukemia within one year	0.10	0.005	1.10	**	0.099	0.010	1.10	**
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.070	0.003	1.07	**	0.070	0.006	1.07	**
Lymphoma within two years	0.075	0.004	1.08	**	0.075	0.008	1.08	**
Metastatic Cancers within one year	0.14	0.003	1.15	**	0.14	0.006	1.15	**
Multiple Myeloma within one year	0.23	0.003	1.26	**	0.23	0.008	1.26	**
Breast, Prostate, Colorectal and Other Cancers within one year	0.067	0.001	1.07	**	0.067	0.003	1.07	**
Hyperparathyroidism within one year	0.033	0.001	1.03	**	0.033	0.002	1.03	**
Monoclonal Gammopathy within one year	0.025	0.004	1.03	**	0.027	0.009	1.03	**
Myelofibrosis within one year	0.10	0.004	1.11	**	0.10	0.010	1.11	**
Myelodysplastic Syndrome between 1999-2004	0.20	0.003	1.22	**	0.20	0.006	1.22	**
Census region fixed effects					yes			
Time trends					yes			
R^2		6.18%				1.37%		
N (pat-mon-fac records)					7,188,698			

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 2-6. Results from three lagged effect models

Variables	Dependent Variable								
	1-month lead SB MAP/month			2-month lead SB MAP/month			3-month lead SB MAP/month		
Independent variable of interest									
Number of skipped sessions	18.01	**	1.32	18.91	**	1.36	19.41	**	1.40
Demographic variables									
Ages <18 yrs	165.08	**	9.58	164.02	**	10.00	163.28	**	10.44
Ages 18-44 yrs	106.86	**	1.01	99.98	**	1.04	94.95	**	1.07
Ages 45-59 yrs	41.22	**	0.81	37.78	**	0.83	35.22	**	0.86
Ages 60-69 yrs (ref.)	ref.		-	-		-	-		-
Ages 70-79 yrs	-58.03	**	0.82	-56.42	**	0.84	-55.43	**	0.86
Ages 80+ yrs	-102.63	**	1.00	-100.01	**	1.03	-98.43	**	1.07
Female	99.00	**	0.62	100.36	**	0.64	100.27	**	0.66
Race: Native American	-42.39	**	2.33	-44.82	**	2.39	-45.66	**	2.45
Race: Asian	21.21	**	1.61	19.45	**	1.65	19.29	**	1.70
Race: Black	94.75	**	0.64	92.64	**	0.66	91.87	**	0.68
Race: White or Unknown/missing (ref.)	ref.		-	-		-	-		-
Race: Other	7.87	**	2.72	6.68	*	2.79	6.81	*	2.87
Patient characteristics and Comorbidities									
Started RRT during month	420.93	**	3.69	262.57	**	3.86	115.76	**	4.03
1 previous month of RRT	298.86	**	2.36	135.90	**	2.47	37.72	**	2.56
2 previous months of RRT	137.90	**	2.34	34.61	**	2.43	-4.37		2.52
3 previous months of RRT	46.38	**	2.09	5.11	*	2.16	-5.69	*	2.22
4 previous months of RRT	1.55		2.13	-11.71	**	2.19	-29.98	**	2.26
5 previous months of RRT	-15.60	**	2.12	-36.47	**	2.18	-63.01	**	2.25
6 previous months of RRT	-45.44	**	2.17	-73.54	**	2.24	-84.56	**	2.31
7 previous months of RRT	-75.77	**	2.16	-87.34	**	2.22	-90.59	**	2.29
8 previous months of RRT	-89.31	**	2.21	-94.24	**	2.28	-100.29	**	2.35
9 previous months of RRT	-96.02	**	2.23	-102.78	**	2.30	-104.27	**	2.37
10-12 previous months of RRT	-107.68	**	1.35	-107.89	**	1.38	-107.48	**	1.42
2nd year of RRT	-88.42	**	0.80	-86.20	**	0.82	-83.34	**	0.85
3rd year of RRT	-54.89	**	0.85	-53.06	**	0.87	-51.29	**	0.90
3 years or more of RRT (ref.)	ref.		-	-		-	-		-
Body surface area (Dubois formula)	279.84	**	1.33	282.18	**	1.37	279.67	**	1.41
Underweight (BMI <18.5 kg/m^2)	14.09	**	1.47	12.67	**	1.53	10.43	**	1.59
Inability to ambulate (2728)	25.38	**	1.78	27.97	**	1.85	28.36	**	1.92
Smoking	-34.63	**	1.59	-32.99	**	1.65	-32.18	**	1.71
Alcohol Dependence between 1999-2004	59.62	**	1.29	59.66	**	1.33	60.72	**	1.37
Drug Dependence between 1999-2004	42.72	**	1.43	41.48	**	1.48	41.83	**	1.53
Cardiac Arrest within one year	80.12	**	2.60	61.66	**	2.71	49.44	**	2.83
Cardiac dysrhythmia within one year	73.03	**	0.64	64.44	**	0.66	58.76	**	0.68
Ischemic heart disease within one year	39.52	**	0.64	36.43	**	0.65	34.75	**	0.67
Pericarditis within one year	123.63	**	2.73	108.93	**	2.81	98.30	**	2.90
Cerebrovascular disease within one year	17.89	**	0.68	14.23	**	0.70	12.87	**	0.72

Diabetes within one year	35.82	**	0.62	34.07	**	0.64	34.33	**	0.66
Peripheral vascular disease within one year	56.54	**	0.60	49.45	**	0.62	46.00	**	0.64
Chronic obstructive pulmonary disease within one year	59.65	**	0.65	53.96	**	0.67	50.83	**	0.69
Acquired immunodeficiency disease within one year	132.80	**	3.44	134.83	**	3.53	134.29	**	3.63
Human immnodeficiency virus within one year	82.99	**	3.90	76.67	**	4.01	73.78	**	4.11
Bacterial Pneumonia six months ago	23.10	**	4.62	22.02	**	4.81	16.44	**	5.02
Hepatitis B within one year	31.30	**	2.58	27.60	**	2.66	25.51	**	2.74
Other Hepatitis between 1999-2004	-40.32	**	1.13	-40.31	**	1.16	-39.34	**	1.19
Opportunistic Infection six months ago	88.75	**	7.92	79.55	**	8.23	70.35	**	8.53
Pneumococcal pneumonia, emphysema, lung abcess within six months	39.94	**	6.64	35.83	**	6.88	33.42	**	7.12
Septicemia within six months	81.93	**	1.53	70.32	**	1.58	64.58	**	1.64
Gastro-Intestinal (GI) Tract Bleeding six months ago	127.70	**	4.80	112.35	**	4.98	110.92	**	5.16
GI Ulcer - no hemorrhage within six months	45.14	**	3.68	46.31	**	3.80	44.83	**	3.93
Esophogeal Varices within six months	307.98	**	13.89	279.89	**	14.53	276.87	**	15.28
Acquired Hemolytic Anemias within one year	30.10	**	2.47	25.63	**	2.55	17.82	**	2.63
Hereditary Hemolytic Anemias between 1999-2004	108.34	**	2.10	106.75	**	2.16	105.33	**	2.24
Sickle-Cell Anemia between 1999-2004	234.72	**	4.35	235.61	**	4.49	231.04	**	4.63
Leukemia within one year	119.68	**	4.29	117.41	**	4.47	115.47	**	4.66
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	78.47	**	2.64	74.56	**	2.76	68.82	**	2.89
Lymphoma within two years	83.32	**	3.42	81.77	**	3.55	80.01	**	3.69
Metastatic Cancers within one year	160.21	**	2.67	151.68	**	2.81	139.45	**	2.94
Multiple Myeloma within one year	277.59	**	3.16	275.45	**	3.30	268.80	**	3.45
Breast, Prostate, Colorectal and Other Cancers within one year	58.38	**	1.07	56.78	**	1.11	55.41	**	1.14
Hyperparathyroidism within one year	22.40	**	0.93	16.51	**	0.96	12.10	**	0.98
Monoclonal Gammopathy within one year	23.38	**	3.67	22.62	**	3.81	24.55	**	3.94
Myelofibrosis within one year	118.67	**	4.04	112.61	**	4.16	107.55	**	4.28
Myelodysplastic Syndrome between 1999-2004	257.62	**	2.61	253.52	**	2.72	250.51	**	2.82
Census region fixed effects				yes					
Time trends				yes					
R^2	6.20%			5.52%			5.26%		
N (pat-mon-fac records)	6,772,535			6,381,413			6,013,770		

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 2-7. Sensitivity analysis: OLS and 2SLS regression results after the exclusion of month of death and the month prior to death

Variables	Dependent variable: SB MAP/month					
	OLS (1)			IV-2SLS (2)		
	Coeff.		S.E.	Coeff.		S.E.
Independent variable of interest						
Number of skipped sessions	-68.58	**	1.3	-2254.71	**	178.61
Demographic variables						
Ages <18 yrs	175.33	**	9.38	179.37	**	11.13
Ages 18-44 yrs	129.14	**	1.01	127.34	**	1.19
Ages 45-59 yrs	49.45	**	0.81	48.72	**	0.96
Ages 60-69 yrs (ref.)	ref.		-	-		-
Ages 70-79 yrs	-63.89	**	0.81	-63.77	**	0.96
Ages 80+ yrs	-111.03	**	1	-111.02	**	1.18
Female	101.93	**	0.62	101.97	**	0.73
Race: Native American	-37.14	**	2.31	-37.30	**	2.74
Race: Asian	18.73	**	1.59	18.73	**	1.89
Race: Black	98.46	**	0.64	97.13	**	0.76
Race: White or Unknown/missing (ref.)	ref.		-	-		-
Race: Other	9.21	**	2.71	8.68	**	3.21
Patient characteristics and Comorbidities						
Started RRT during month	-128.63	**	3.77	-126.50	**	4.48
1 previous month of RRT	411.43	**	2.36	410.15	**	2.80
2 previous months of RRT	343.53	**	2.33	342.13	**	2.76
3 previous months of RRT	179.89	**	2.08	177.96	**	2.47
4 previous months of RRT	60.59	**	2.12	58.63	**	2.51
5 previous months of RRT	8.51	**	2.11	6.54	**	2.50
6 previous months of RRT	-17.86	**	2.16	-19.87	**	2.56
7 previous months of RRT	-41.15	**	2.14	-43.18	**	2.54
8 previous months of RRT	-73.18	**	2.2	-75.23	**	2.61
9 previous months of RRT	-90.26	**	2.22	-92.25	**	2.63
10-12 previous months of RRT	-104.76	**	1.34	-106.87	**	1.59
2nd year of RRT	-90.73	**	0.8	-92.58	**	0.95
3rd year of RRT	-57.51	**	0.85	-58.81	**	1.00
3 years or more of RRT (ref.)	ref.		-	-		-
Body surface area (Dubois formula)	278.78	**	1.32	280.27	**	1.57
Underweight (BMI <18.5 kg/m^2)	26.36	**	1.47	26.00	**	1.74
Inability to ambulate (2728)	24.62	**	1.77	24.76	**	2.10
Smoking	-36.80	**	1.56	-38.25	**	1.86
Alcohol Dependence between 1999-2004	67.22	**	1.28	65.64	**	1.52
Drug Dependence between 1999-2004	59.03	**	1.42	58.10	**	1.68
Cardiac Arrest within one year	103.56	**	2.59	103.91	**	3.08
Cardiac dysrhythmia within one year	89.95	**	0.64	90.26	**	0.76
Ischemic heart disease within one year	48.75	**	0.63	48.98	**	0.75

Pericarditis within one year	149.27	**	2.71	149.52	**	3.22
Cerebrovascular disease within one year	26.93	**	0.67	27.19	**	0.80
Diabetes within one year	42.51	**	0.62	43.22	**	0.73
Peripheral vascular disease within one year	73.71	**	0.6	74.00	**	0.71
Chronic obstructive pulmonary disease within one year	74.08	**	0.65	74.04	**	0.77
Acquired immunodeficiency disease within one year	137.58	**	3.41	137.03	**	4.04
Human immnodeficiency virus within one year	97.20	**	3.88	96.64	**	4.60
Bacterial Pneumonia six months ago	35.29	**	4.63	35.63	**	5.49
Hepatitis B within one year	43.22	**	2.57	43.20	**	3.04
Other Hepatitis between 1999-2004	-38.50	**	1.12	-38.65	**	1.33
Opportunistic Infection six months ago	115.96	**	7.89	116.34	**	9.36
Pneumococcal pneumonia, emphysema, lung abcess within six months	39.07	**	6.65	39.40	**	7.90
Septicemia within six months	111.50	**	1.53	111.44	**	1.81
Gastro-Intestinal (GI) Tract Bleeding six months ago	155.29	**	4.81	155.24	**	5.70
GI Ulcer - no hemorrhage within six months	56.75	**	3.67	56.73	**	4.35
Esophogeal Varices within six months	336.83	**	13.8	337.02	**	16.37
Acquired Hemolytic Anemias within one year	51.73	**	2.45	52.23	**	2.91
Hereditary Hemolytic Anemias between 1999-2004	112.23	**	2.08	112.55	**	2.47
Sickle-Cell Anemia between 1999-2004	251.32	**	4.32	251.52	**	5.12
Leukemia within one year	129.27	**	4.28	129.45	**	5.08
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	92.18	**	2.64	92.15	**	3.14
Lymphoma within two years	92.16	**	3.4	92.23	**	4.03
Metastatic Cancers within one year	184.12	**	2.68	184.05	**	3.18
Multiple Myeloma within one year	295.17	**	3.16	295.33	**	3.75
Breast, Prostate, Colorectal and Other Cancers within one year	63.51	**	1.07	63.88	**	1.27
Hyperparathyroidism within one year	31.47	**	0.93	31.60	**	1.10
Monoclonal Gammopathy within one year	25.47	**	3.66	26.19	**	4.34
Myelofibrosis within one year	136.04	**	4.03	136.60	**	4.78
Myelodysplastic Syndrome between 1999-2004	265.17	**	2.6	265.44	**	3.08
Census region fixed effects			yes			
Time trends			yes			
R^2	7.54%			5.45%		
N (pat-mon-fac records)			6,969,739			

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

** Significantly different from zero at 99 percent confidence.

Table 2-7. Sensitivity analysis: OLS and 2SLS regression results after the exclusion of month of death and the month prior to death (cont'd)

Variables	Dependent variable: log (SB MAP/month)							
	OLS (3)				IV-2SLS (4)			
	Coeff.	S.E.	Mult.		Coeff.	S.E.	Mult.	
Independent variable of interest								
Number of skipped sessions	-0.096	0.001	0.91	**	-7.41	0.36	0.0006	**
Demographic variables								
Ages <18 yrs	-0.041	0.011	0.96	**	-0.031	0.023	0.97	
Ages 18-44 yrs	0.089	0.0011	1.09	**	0.087	0.002	1.09	**
Ages 45-59 yrs	0.024	0.0009	1.02	**	0.023	0.002	1.02	**
Ages 60-69 yrs (ref.)	ref.	-	-		-	-	-	
Ages 70-79 yrs	-0.051	0.0009	0.95	**	-0.051	0.002	0.95	**
Ages 80+ yrs	-0.092	0.0011	0.91	**	-0.093	0.002	0.91	**
Female	0.124	0.0007	1.13	**	0.12	0.001	1.13	**
Race: Native American	-0.024	0.0026	0.98	**	-0.023	0.006	0.98	**
Race: Asian	0.041	0.0018	1.04	**	0.040	0.004	1.04	**
Race: Black	0.132	0.0007	1.14	**	0.13	0.002	1.14	**
Race: White or Unknown/missing (ref.)	ref.	-	-		-	-	-	
Race: Other	0.035	0.0031	1.04	**	0.033	0.007	1.03	**
Patient characteristics and Comorbidities								
Started RRT during month	-0.19	0.0043	0.82	**	-0.19	0.009	0.83	**
1 previous month of RRT	0.43	0.0027	1.54	**	0.43	0.006	1.54	**
2 previous months of RRT	0.36	0.0026	1.43	**	0.36	0.006	1.43	**
3 previous months of RRT	0.18	0.0024	1.20	**	0.18	0.005	1.19	**
4 previous months of RRT	0.054	0.0024	1.06	**	0.051	0.005	1.05	**
5 previous months of RRT	0.014	0.0024	1.01	**	0.011	0.005	1.01	*
6 previous months of RRT	0.002	0.0024	1.00		-0.0005	0.005	1.00	
7 previous months of RRT	-0.018	0.0024	0.98	**	-0.021	0.005	0.98	**
8 previous months of RRT	-0.057	0.0025	0.94	**	-0.059	0.005	0.94	**
9 previous months of RRT	-0.075	0.0025	0.93	**	-0.077	0.005	0.93	**
10-12 previous months of RRT	-0.087	0.0015	0.92	**	-0.090	0.003	0.91	**
2nd year of RRT	-0.075	0.0009	0.93	**	-0.078	0.002	0.92	**
3rd year of RRT	-0.042	0.0010	0.96	**	-0.044	0.002	0.96	**
3 years or more of RRT (ref.)	ref.	-	-		-	-	-	
Body surface area (Dubois formula)	0.26	0.0015	1.30	**	0.27	0.003	1.31	**
Underweight (BMI <18.5 kg/m^2)	0.013	0.0017	1.01	**	0.013	0.004	1.01	**
Inability to ambulate (2728)	0.018	0.0020	1.02	**	0.019	0.004	1.02	**
Smoking	-0.043	0.0018	0.96	**	-0.045	0.004	0.96	**
Alcohol Dependence between 1999-2004	0.070	0.0014	1.07	**	0.067	0.003	1.07	**
Drug Dependence between 1999-2004	0.057	0.0016	1.06	**	0.056	0.003	1.06	**
Cardiac Arrest within one year	0.080	0.0029	1.08	**	0.081	0.006	1.08	**
Cardiac dysrhythmia within one year	0.080	0.0007	1.08	**	0.080	0.002	1.08	**
Ischemic heart disease within one year	0.055	0.0007	1.06	**	0.056	0.002	1.06	**

Pericarditis within one year	0.13	0.0031	1.13	**	0.13	0.007	1.13	**
Cerebrovascular disease within one year	0.025	0.0008	1.03	**	0.026	0.002	1.03	**
Diabetes within one year	0.060	0.0007	1.06	**	0.061	0.001	1.06	**
Peripheral vascular disease within one year	0.065	0.0007	1.07	**	0.065	0.001	1.07	**
Chronic obstructive pulmonary disease within one year	0.067	0.0007	1.07	**	0.067	0.002	1.07	**
Acquired immunodeficiency disease within one year	0.12	0.0038	1.13	**	0.12	0.008	1.13	**
Human immnodeficiency virus within one year	0.080	0.0044	1.08	**	0.079	0.009	1.08	**
Bacterial Pneumonia six months ago	0.022	0.0052	1.02	**	0.023	0.011	1.02	*
Hepatitis B within one year	0.037	0.0029	1.04	**	0.037	0.006	1.04	**
Other Hepatitis between 1999-2004	-0.052	0.0013	0.95	**	-0.052	0.003	0.95	**
Opportunistic Infection six months ago	0.089	0.0089	1.09	**	0.089	0.019	1.09	**
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.031	0.0075	1.03	**	0.032	0.016	1.03	*
Septicemia within six months	0.085	0.0017	1.09	**	0.086	0.004	1.09	**
Gastro-Intestinal (GI) Tract Bleeding six months ago	0.12	0.0054	1.13	**	0.12	0.012	1.13	**
GI Ulcer - no hemorrhage within six months	0.047	0.0041	1.05	**	0.047	0.009	1.05	**
Esophogeal Varices within six months	0.27	0.0156	1.31	**	0.27	0.033	1.31	**
Acquired Hemolytic Anemias within one year	0.006	0.0028	1.01	*	0.007	0.006	1.01	
Hereditary Hemolytic Anemias between 1999-2004	0.088	0.0023	1.09	**	0.089	0.005	1.09	**
Sickle-Cell Anemia between 1999-2004	0.17	0.0049	1.18	**	0.17	0.010	1.18	**
Leukemia within one year	0.10	0.0048	1.10	**	0.10	0.010	1.10	**
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.072	0.0030	1.07	**	0.072	0.006	1.07	**
Lymphoma within two years	0.077	0.0038	1.08	**	0.077	0.008	1.08	**
Metastatic Cancers within one year	0.14	0.0030	1.15	**	0.14	0.006	1.16	**
Multiple Myeloma within one year	0.23	0.0036	1.26	**	0.23	0.008	1.26	**
Breast, Prostate, Colorectal and Other Cancers within one year	0.067	0.0012	1.07	**	0.067	0.003	1.07	**
Hyperparathyroidism within one year	0.033	0.0010	1.03	**	0.033	0.002	1.03	**
Monoclonal Gammopathy within one year	0.026	0.0041	1.03	**	0.027	0.009	1.03	**
Myelofibrosis within one year	0.10	0.0045	1.11	**	0.10	0.010	1.11	**
Myelodysplastic Syndrome between 1999-2004	0.20	0.0029	1.22	**	0.20	0.006	1.22	**
Census region fixed effects				yes				
Time trends				yes				
R^2		6.29%				1.43%		
N (pat-mon-fac records)				6,969,739				

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 2-8. Sensitivity analysis: Results from three lagged effect models after the exclusion of month of death and the month prior to death

Variables	Dependent Variable								
	1-month lead SB MAP/month			2-month lead SB MAP/month			3-month lead SB MAP/month		
Independent variable of interest									
Number of skipped sessions	19.80	**	1.33	20.66	**	1.37	20.97	**	1.41
Demographic variables									
Ages <18 yrs	166.53	**	9.58	162.32	**	9.99	162.84	**	10.43
Ages 18-44 yrs	106.79	**	1.02	99.64	**	1.05	94.51	**	1.07
Ages 45-59 yrs	40.93	**	0.82	37.52	**	0.84	34.95	**	0.86
Ages 60-69 yrs (ref.)	ref.		-	-		-	-		
Ages 70-79 yrs	-57.46	**	0.83	-55.63	**	0.85	-54.78	**	0.87
Ages 80+ yrs	-99.98	**	1.02	-97.47	**	1.05	-96.11	**	1.09
Female	99.72	**	0.63	101.04	**	0.65	101.05	**	0.66
Race: Native American	-41.66	**	2.35	-43.90	**	2.41	-44.80	**	2.47
Race: Asian	20.11	**	1.62	18.52	**	1.66	18.32	**	1.71
Race: Black	94.57	**	0.65	92.50	**	0.67	91.67	**	0.69
Race: White or Unknown/missing (ref.)	ref.		-	-		-	-		-
Race: Other	8.35	**	2.74	6.79	*	2.82	6.71	*	2.90
Patient characteristics and Comorbidities									
Started RRT during month	440.14	**	3.78	272.40	**	3.94	116.83	**	4.10
1 previous month of RRT	312.26	**	2.41	139.83	**	2.51	39.12	**	2.61
2 previous months of RRT	142.70	**	2.39	36.11	**	2.48	-4.74		2.56
3 previous months of RRT	47.65	**	2.12	5.58	*	2.19	-6.00	**	2.25
4 previous months of RRT	1.46		2.16	-12.16	**	2.22	-30.78	**	2.29
5 previous months of RRT	-16.56	**	2.14	-37.62	**	2.21	-63.25	**	2.28
6 previous months of RRT	-47.14	**	2.20	-73.89	**	2.26	-85.82	**	2.33
7 previous months of RRT	-76.30	**	2.18	-88.47	**	2.25	-92.46	**	2.32
8 previous months of RRT	-90.73	**	2.24	-96.67	**	2.31	-100.63	**	2.38
9 previous months of RRT	-98.63	**	2.26	-103.21	**	2.32	-107.45	**	2.40
10-12 previous months of RRT	-109.86	**	1.36	-110.52	**	1.40	-109.95	**	1.44
2nd year of RRT	-90.37	**	0.81	-88.27	**	0.83	-85.08	**	0.86
3rd year of RRT	-55.99	**	0.86	-54.01	**	0.88	-52.24	**	0.91
3 years or more of RRT (ref.)	ref.		-	-		-	-		-
Body surface area (Dubois formula)	279.67	**	1.34	281.97	**	1.38	279.47	**	1.42
Underweight (BMI <18.5 kg/m^2)	17.17	**	1.50	14.99	**	1.56	12.57	**	1.61
Inability to ambulate (2728)	27.94	**	1.81	30.06	**	1.88	30.01	**	1.96
Smoking	-34.53	**	1.60	-32.64	**	1.66	-32.21	**	1.73
Alcohol Dependence between 1999-2004	59.99	**	1.30	59.92	**	1.34	60.95	**	1.39
Drug Dependence between 1999-2004	44.30	**	1.45	42.99	**	1.50	43.06	**	1.55
Cardiac Arrest within one year	86.06	**	2.67	66.38	**	2.78	54.13	**	2.89
Cardiac dysrhythmia within one year	75.54	**	0.65	66.66	**	0.67	60.97	**	0.69
Ischemic heart disease within one year	40.71	**	0.64	37.47	**	0.66	35.85	**	0.68
Pericarditis within one year	125.24	**	2.76	109.78	**	2.85	98.33	**	2.94

Cerebrovascular disease within one year	19.25	**	0.69	15.66	**	0.71	14.22	**	0.73
Diabetes within one year	36.98	**	0.63	35.24	**	0.64	35.46	**	0.66
Peripheral vascular disease within one year	57.86	**	0.61	50.70	**	0.63	47.08	**	0.65
Chronic obstructive pulmonary disease within one year	61.73	**	0.66	56.04	**	0.68	52.84	**	0.70
Acquired immunodeficiency disease within one year	132.55	**	3.46	134.28	**	3.55	134.24	**	3.65
Human immnodeficiency virus within one year	83.22	**	3.93	77.25	**	4.03	73.49	**	4.14
Bacterial Pneumonia six months ago	26.04	**	4.75	25.66	**	4.94	16.97	**	5.14
Hepatitis B within one year	32.07	**	2.61	27.51	**	2.69	24.96	**	2.77
Other Hepatitis between 1999-2004	-40.81	**	1.14	-40.67	**	1.17	-39.93	**	1.20
Opportunistic Infection six months ago	91.81	**	8.08	79.77	**	8.38	71.18	**	8.68
Pneumococcal pneumonia, emphysema, lung abcess within six months	40.07	**	6.79	32.80	**	7.02	33.89	**	7.27
Septicemia within six months	83.96	**	1.56	71.76	**	1.61	65.80	**	1.67
Gastro-Intestinal (GI) Tract Bleeding six months ago	129.05	**	4.91	112.87	**	5.08	111.79	**	5.26
GI Ulcer - no hemorrhage within six months	48.10	**	3.74	45.45	**	3.86	44.54	**	3.99
Esophogeal Varices within six months	310.45	**	14.28	288.14	**	14.94	276.25	**	15.63
Acquired Hemolytic Anemias within one year	29.87	**	2.50	25.14	**	2.58	17.67	**	2.66
Hereditary Hemolytic Anemias between 1999-2004	108.37	**	2.12	107.14	**	2.19	105.95	**	2.26
Sickle-Cell Anemia between 1999-2004	235.53	**	4.40	236.23	**	4.54	232.42	**	4.68
Leukemia within one year	120.38	**	4.40	118.64	**	4.57	115.64	**	4.75
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	83.03	**	2.73	77.14	**	2.85	70.91	**	2.97
Lymphoma within two years	86.61	**	3.48	84.71	**	3.62	82.24	**	3.75
Metastatic Cancers within one year	165.44	**	2.77	154.57	**	2.90	141.43	**	3.04
Multiple Myeloma within one year	278.26	**	3.26	273.83	**	3.39	266.36	**	3.54
Breast, Prostate, Colorectal and Other Cancers within one year	58.92	**	1.09	56.74	**	1.12	55.36	**	1.16
Hyperparathyroidism within one year	22.18	**	0.94	16.25	**	0.97	11.68	**	0.99
Monoclonal Gammopathy within one year	24.56	**	3.74	23.43	**	3.87	24.53	**	4.01
Myelofibrosis within one year	119.17	**	4.10	112.73	**	4.21	107.35	**	4.33
Myelodysplastic Syndrome between 1999-2004	256.50	**	2.66	253.26	**	2.77	249.78	**	2.88
Census region fixed effects				yes					
Time trends				yes					
R^2	6.33%			5.61%			5.34%		
N (pat-mon-fac records)	6,586,921			6,210,882			5,855,789		

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 36 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan status.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

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Chapter III

Chapter III. Examining the Association between Non-Adherence and Composite Rate Costs for Hemodialysis Facilities

Abstract

Background. The substantial body of studies exploring the relationship of non-adherence in hemodialysis (HD) sessions to the patients' outcome and quality of life has rarely investigated the economic consequences within the end-stage renal disease (ESRD) community. While a few existing studies have examined the relationship between non-adherence with ESRD medical expenditure, none has investigated this relationship at the dialysis facility level.

Objectives. This study investigates whether there is an association between non-adherence, as measured by the average HD sessions missed per patient per month, and composite rate (CR) costs for dialysis facilities, using a nationally representative sample.

Methods. The study population includes 11,600 facility-years from between the years 2004 and 2006. The sources of the CR cost data are the Medicare Independent Renal Dialysis Facility Cost Reports (Form CMS 265-94) and the Medicare Hospital Cost Reports (Form CMS 2552-96). Patient characteristics, comorbidities, and factors

associated with an interrupted dialysis month, such as missed sessions, transfer between facility, hospitalization, and transplantation, were measured using CMS Form 2728 and/or Medicare claims. Since CR costs were right-skewed, we examined the association using both OLS and log-linear models and compared the coefficient estimates derived from each. In addition, this study investigates whether the inclusion of facility control variables significantly changes the effect.

Results. Descriptive statistics show that the average CR cost per month was $2,089.50 between 2004 and 2006. The average dialysis sessions missed per patient per month at the facility level is 0.11. Without facility control variables, the coefficient estimate of non-adherence was not statistically significant in the OLS model, with an R-square of 1.59 percent. The coefficient estimate from the log-linear model was 0.066 (p=0.0059; multiplier=1.07), with an R-square of 15.48 percent. After the inclusion of facility control variables, the OLS coefficient estimate of non-adherence remained insignificant. The R-square increased to 3.37 percent. In the log-linear model with facility control variables, the coefficient estimate of non-adherence was also insignificant, although the R-square increased dramatically to 39.44 percent.

Conclusion. This study did not find an association between non-adherence and CR costs at the dialysis facility level, except for the log-linear model without facility control variables. Since there are no meaningful cost savings for dialysis facilities when patients skipped routine HD treatments, combined with the revenue loss facing these facilities when patients do not show up for their appointments, there is a financial incentive for dialysis facilities to improve patient adherence. In order to improve adherence, dialysis facilities could consider using various approaches, e.g., reminder phone calls, text

messages, and e-mails, to target patients who are more likely to skip sessions. A policy intervention from the CMS may not be necessary at this time .

Key Words. Non-adherence, health care costs, hemodialysis, dialysis facility, ESRD

Introduction

This study provides information on whether non-adherence in HD sessions is associated with short-run composite rate costs. Specifically, in the OLS and log-linear regression models of CR costs on non-adherence, when controlling for patient case-mix factors and/or facility characteristics, no association was found between non-adherence and CR costs.

CR costs include the all-inclusive payments for a comprehensive bundle of institutional and home dialysis services, which may consist of nursing services supplies, equipment, drugs, and administrative efforts associated with dialysis treatments (Rettig et al., 1990). In general, in-center HD sessions are administered three times per week for each HD patient, with three to four hours of dialysis per session. There are usually three shifts of dialysis patients per day. The ESRD industry does not overbook HD patients, unlike other industries such as the airline industry, which adopts an overbooking strategy to control for the damage on economic costs when a passenger does not show up. Therefore, when an HD patient misses his appointment randomly, the fixed cost component, e.g., nursing and administrative staff, of the CR costs would need to be absorbed by the dialysis facility. Results from this study might be useful for both dialysis facilities and the CMS. From the dialysis facilities' perspective, they could implement

strategies to increase the adherence rate if the results show that non-adherence is associated with higher CR costs. From the CMS's perspective, it is important to know what the magnitude of non-adherence on CR costs is, in order to better monitor reimbursement and regulate budgetary issues.

Although an extensive body of literature exists to explore the effect of non-adherence on a myriad of factors—such as its association with patient-specific characteristics and with patient outcomes—none has specifically assessed the impact of missed HD sessions on CR costs for dialysis facilities. In terms of the assessment on data issues and methodologies used by previous non-adherence studies, there are two common limitations that constrain their reliability and validity. Most studies use cross-sectional data to conduct analysis, failing to control for plausible temporal trends that may be associated with the dependent variable. To address this concern, this study uses longitudinal panel data from 2004 to 2006. Another issue is related to the sample size and sampling strategies. Most of the literature on non-adherence of HD sessions used a relatively small number of study observations, which limits generalizability. This study uses data on all in-center HD facilities in the United States without any missing values in covariates as the unit of analysis.

Literature Review

Within the ESRD literature, issues concerning patient non-adherence with HD prescriptions have been discussed extensively. A large body of research regarding predictors and clinical outcomes of non-adherence has been published in the clinical

literature (Denhaerynck et al., 2005; Jarzembowski et al., 2004; Leggat et al., 1998; Leggat et al., 2005; Saran et al., 2003). Most researchers define non-adherence in dialysis patients when there is an interdialytic weight gain >1.5 kg, a serum phosphorus level >6 mg/dL, and/or a predialysis serum potassium level >5.5 mEq/L, or when dialysis sessions are shortened or missed by the patient. Many studies found a positive correlation between non-adherence in dialysis sessions and worsening health outcomes, and a negative association between non-adherence and quality of life (Denhaerynck et al., 2005; Leggat et al., 1998; Saran et al., 2003). Nevertheless, it is surprising to find that the economic consequences of non-adherence have rarely been investigated in the ESRD community. Only a few studies have applied cost-effectiveness or cost-utility analyses to estimate the economic impact of non-adherence in renal transplant patients. For example, Swanson and colleagues (1992) estimated that the non-adherence related additional hospital cost, after transplantation, amounts to $900 per non-adherent patient per year. Cleemput and colleagues (2004) conducted cost-utility analyses to assess non-adherence and its economic consequences in a renal transplant population and found that non-adherent recipients' lifetime treatment costs were actually lower, due to lower life expectancies.

It is important to understand whether non-adherence has a significant impact on dialysis costs facing the current cost-conscious U.S. health care environment. In 1973, the Medicare ESRD Program was established as a national health insurance program for eligible residents diagnosed with end-stage renal disease. Over the past few decades, the total number of prevalent dialysis patients and the total expenditure of the ESRD program have continuously increased. In 2007, there were 506,256 prevalent ESRD patients in the

U.S. The medical expenditures associated with treating these patients have reached $20 billion, accounting for 6.4% of the Medicare budget (U.S. Renal Data System [USRDS] 2007). The improved mortality rates of prevalent ESRD patients and the continuing growth of incident ESRD patients both contribute to the rising cost pressures encountered by the CMS.

Non-adherence is commonly observed in dialysis patients (Curtin et al., 1999; Leggat et al., 1998). Although dialysis is lifesaving, it only replaces 10 percent of normal renal function. Patients may continue to encounter many medical problems such as salt and water retention, hyperparathyroidism, hypertension, and heart disease, among others (Loghman-Adham, 2003). On average, dialysis patients need to take medication 6 to 10 times per day (Loghman-Adham, 2003). It takes a considerable amount of discipline and determination for patients to adhere to routine sessions and properly take the prescribed medications. The non-adherence issue is particularly important for those living in the United States. Bleyer and colleagues' (1999) studies on international comparisons of patient adherence on hemodialysis found that roughly 2.3% of dialysis sessions were missed by patients in the United States, whereas missed dialysis treatments were virtually nonexistent in Japan and Sweden.

There are wide variations in terms of what constitutes non-adherence. How researchers define their non-adherence measures would affect the estimated prevalence and associated mortality risks (Kimmel et al., 1998; Kimmel et al., 1995; Leggat et al., 1998; Saran et al., 2003). Based on these definitions, the prevalence of non-adherence has been reported to vary from as little as 2% to as much as 100% (Leggat, 2005). Because different definitions were employed, it is difficult to make direct comparisons

across studies. Results of predictors of non-adherence are mixed. Most studies show that predictors in adult HD patients include age, race, sex, marital status, socioeconomic status, and educational level (Bame et al., 1993; Brownbridge et al., 1994; Gordon et al., 2003; Hoover, 1989; Morduchowicz et al., 1993). However, Leggat and colleagues (1998) did not find sex or education level statistically significant.

Most studies examining the issues regarding missed and shortened HD sessions focused on patient characteristics and individual reasons leading to non-adherence (Gordon et al., 2003; Loghman-Adham, 2003). In general, younger patients, incident patients, low-income patients, African-Americans, and males are more likely to be associated with non-adherent behaviors. Reasons for non-adherence may include medical problems, life tasks, and difficulty in transportation. Conclusions drawn from these studies often emphasized the development of interventions to target patient-specific characteristics in order to improve the adherence of HD sessions. In terms of outcomes research of non-adherence on dialysis patients, recent studies by Leggat and colleagues (1998), Loghman-Adham (2003), and Saran and colleagues (2003) have shown that non-adherence with HD treatment is associated with increased mortality risk. Missed or shortened dialysis sessions can reduce dialysis adequacy, a potential factor for increased mortality. A majority of dialysis patients suffer from anemia problems related to erythropoietin (EPO) deficiency and require renal anemia management. It has been shown that untreated or under-treated anemia in the dialysis population is associated with increased morbidity and mortality (Tong et al., 2001).

Summarizing non-adherence studies within the ESRD transplantation literature, Denhaerynck and colleagues (2005) concluded that non-adherence in adult renal

transplant patients is associated with poor clinical outcomes. However, non-adherence results in lower life-time costs because of shorter survival as well as lower quality adjusted life years. Consistent determinants of non-adherence were age, social isolation, health beliefs, and health cognition. Jarzembowski and colleagues (2004) examined pediatric patients who received renal transplantation and found that African-American recipients had a significantly higher rate of graft loss when compared to Caucasian and Hispanic recipients. They drew the conclusion that non-adherence is a problem of great importance in the African-American pediatric transplant population. In contrast to the excellent long-term survival rate in pediatric receipts of renal transplantation, Ettenger and colleagues (2005) found that the long-term transplant outcome in adolescents were disappointing because of non-adherence with immunosuppressive medications. With early identification and appropriate interventions, significant improvement in adolescent graft survival is highly possible.

There are several studies that investigated the impact of non-adherence with medication regimens on health care costs (Coambs et al., 1995; Sullivan et al., 1990). Cleemput and colleagues (2002) provided a comprehensive literature review on the economics of non-adherence of therapeutic treatments and concluded that non-adherence is often associated with increased morbidity and mortality for chronic patients. Studies from Iskedjian and colleagues (1998), Sullivan and colleagues (1990), and Coambs and colleagues (1995) have all suggested positive correlations between non-adherence in medication and hospitalization admissions. Though it is very difficult to compare study results because of the lack of a gold standard in the assessment of methodology, non-adherence literature seems to support the fact that it is more costly to treat non-adherent

patients than adherent ones. Clearly, the underlying core concept of these studies is based on the idea that higher adherence is desirable.

Non-adherence in medication utilization and refill behavior associated with cost pressure within Medicare, Medicaid, and the VA population has also received considerable attention. Hirth and colleagues (2008) examined the relationship between out-of-pocket spending and cost-related medication underuse of hemodialysis patients across twelve countries. They concluded that drug costs were associated with national drug financing policies as well as the non-adherence rate. Using data on diabetic management, Piette and colleagues (2004) found that VA enrollees, who generally have more generous drug coverage, reported less cost-related medication underuse than patients with no health insurance, patients with Medicare or Medicaid coverage, and even patients with private health insurance. Their study results also suggest that many diabetic patients use less than the required medication and have poorer health, due to cost-related non-adherence. Mojtabai and colleagues (2003) tested the association of prescription drug coverage with adherence to chronic disease medications and the association of cost-related poor adherence with health outcomes among Medicare beneficiaries at various income and out-of-pocket spending levels. Results showed a positive correlation between the lack of drug coverage and cost-related poor adherence. Cost-related poor adherence is related to adverse health outcomes, lower income level, and higher out-of-pocket spending.

Conceptual Framework

We consider a framework in which dialysis facilities are assumed to be profit-maximizing, and will find means to improve patient adherence if the presence of non-adherence reduces profitability. There are two components of costs for CR services, the fixed costs and the variable costs. Fixed costs include capital investments, operational overhead, and labor costs (e.g., nursing staff) associated with managing a dialysis facility. Variable costs are setup costs and supply costs (e.g., drugs).

Suppose there are two dialysis facilities, facility A and facility B, with an equal number of stations. We assume that originally the stations in each facility are constantly full. The fixed costs components are similar at these two facilities. Suppose facility A experiences an exogenous shock in which the number of missed sessions increases over an extended period of time as compared with facility B. Under this scenario, total setup and supply costs are expected to be lower in facility A due to fewer sessions provided, but average setup and supply costs will remain constant. The number of patients receiving dialysis treatments at any given time is different at these two facilities, suggesting different staffing requirements. Because missed sessions are assumed to be unpredictable, staffing arrangement cannot be easily adjusted in the short-run. Hence, the fixed costs per treatment would increase. Combining both fixed costs and variable costs effects, it is hypothesized that the net effect of non-adherence on CR costs per treatment should be positive.

This study attempts to examine the relationship and magnitude of the impact of non-adherence in HD sessions on CR costs. Health economists often use linear models or logarithmic models to estimate health care expenditures, e.g., hospitalization costs. Logarithmic models are useful when dealing with heavy-tailed data, since a log-

transformed dependent variable would better satisfy the assumption of normality under the requirement of linear models. We first examine whether CR costs in this study feature a skewed distribution. Then, since facility characteristics are often important predictors for CR costs, and can be used as either payment or control variables in a bundled case-mix adjusted payment system, we employ OLS and log-linear models, both with and without the inclusion of facility characteristics to assess the effects.

Specific research and policy questions are:

(1) What is the magnitude of impact regarding non-adherence on CR costs at the facility level using both linear and log-linear regression models?

(2) How does controlling for facility characteristics affect the relationship between non-adherence and CR costs?

(3) What are the policy implications with respect to the effect of non-adherence on CR costs?

Methods and Data

Data

The study sample included 11,600 dialysis facility-years between 2004 and 2006. The CR costs for each dialysis patient from the patient-month-facility level dataset were summarized to the facility level. Measures that can vary across month, e.g., missed

sessions and some comorbidities, were summarized at the annual facility-level as an average of their values across months.

The sources of the cost data are the Medicare Independent Renal Dialysis Facility Cost Reports (Form CMS 265-94) and the Medicare Hospital Cost Reports (Form CMS 2552-96). Patient characteristics, comorbidities and factors associated with a partial dialysis month such as missed sessions, transfer between facility, hospitalization and transplantation were measured using CMS Form 2728 and/or Medicare claims.

Variables

Dependent variables

The dependent variable in this study was CR costs per patient per month. Facility costs were based on Medicare allowable costs reported by facilities for dialysis and related services for which they are reimbursed through the composite rate. A second dependent variable used in this study is the log transformation of CR costs.

The cost information for CR services is reported on the Medicare Cost Report from each dialysis facility. Data on the actual costs of delivering CR services are not available at the patient level. In this study, CR costs were measured as the average cost per patient per month. Total CR costs reported on the Cost Report were divided by total treatments for each facility to obtain the average CR costs per treatment. This measure was merged with the patient-month-facility dataset that has individual patient information (e.g., demographics and comorbidities) on dialysis treatments received in each month.

The average CR costs per month for each dialysis patient was derived by multiplying the average CR costs per treatment to the dialysis treatments each patient received during the month. The final measure for the dependent variable was derived by summarizing the average CR costs per month variable from the patient-month-facility level back to the facility level.

Independent variable of interest

The non-adherence measure, the average HD sessions missed per patient per month, was derived using the following strategy. Medicare claims from 2004 to 2006 were selected for analysis only if the number of dialysis sessions was between 0 and 20 for each claim. The average number of HD equivalent dialysis sessions was 12 sessions. Several events that may explain low sessions in HD sessions, including starting month for dialysis with or without hospitalization, transplant with or without hospitalization, death with or without hospitalization, hospitalization only, switching dialysis modality, transfer between facilities, training sessions, and multiple events based on these aforementioned categories, were identified using patient-month-facility level data set.

The measure of missed sessions was then defined as fewer than 12 HD equivalent sessions billed, with none of the above events identified on each record. If the record was identified as a missed month, then the total number of missed sessions for that month was calculated using 12 minus dialysis sessions received for that month. For example, if a dialysis patient was identified as a missed patient in December 2004, and the patient-month-facility record shows that he received eight HD sessions in that month, then the

total number of HD sessions missed in December 2004 is four sessions. The measure of the average HD sessions missed per patient per month was computed by summarizing the number of HD sessions missed from the patient-month-facility data set to the facility-level data set.

Other studies have used different measures for non-adherence. The most common four measures for non-adherence are missed HD sessions, shortened HD sessions by 10 or more minutes, an interdialytic weight gain of more than 5.7 percent, or a serum phosphate of greater than 7.5 mg/Dl (Leggat et. al, 1998). Since this data set did not include information beyond the number of HD sessions missed, an important caveat is the sensitivity of this measure as a proxy to capture the conventional non-adherence measure. Based on a study from Leggat and colleagues (1998), they showed that there was a high degree of correlation among various definitions of non-adherence. For example, if a patient is classified as non-adherent using one definition, e.g., an interdialytic weight gain of more than 5.7 percent, then the odds of this patient being identified as a non-adherent patient using other definitions (e.g., missed sessions) are significantly higher. The strongest correlation was found between missed HD sessions and shortened HD sessions.

Patient characteristics

Several patient characteristics including demographics (age, sex, race), time since start of renal replacement therapy (RRT), body surface area, low body mass index (BMI<18.5 kg/m^2), functional status, and clinical comorbidities that have significant impacts on explaining the variation of CR costs based on prior research (Hirth et al., 2003; Hirth et

al., 2007), were included in the regression models as control variables. Data for the measures of patient characteristics were obtained from the ESRD Medical Evidence Report (CMS Form 2728) and/or Medicare claims. Clinical comorbidities were obtained from both CMS Form 2728 and/or Medicare claims, since evidence shows that there were issues concerning underreporting of comorbidities using only CMS Form 2728. Additionally, this Medical Evidence Report does not capture changes in patients' comorbidities after the initiation of RRT. Comorbid conditions based purely on this form were not perfectly measured. Thus, clinical comorbidity conditions were also based on diagnosis codes reported on various Medicare claims, including inpatient, outpatient, skilled nursing facility, home health, hospice, and physician claims covering a specified period of time.

These claims-based comorbidity measures were limited to recent diagnoses (e.g., during the previous six months only) for acute conditions such as gastrointestinal bleeding. Longer periods were used for chronic conditions. Several "look back" periods (e.g., diagnoses in last year vs. last two years) were tested to determine their ability to predict costs. The most predictive look back period was chosen as the measure of the comorbidity to be entered into the regression models.

Facility characteristics

The relationship between non-adherence and CR costs may be significantly influenced by the inclusion or exclusion of facility characteristics. Therefore, several facility characteristics including hospital-based vs. freestanding, facility size, membership in

major chains, whether a facility is qualified for an exception payment in CR costs, urban vs. rural location, metropolitan status, and census region were also used in the regression models.

Statistical Modeling

Two OLS regression models and two log-linear regression models were estimated to predict CR costs. Model 1 (Equation 3-1) predicted CR costs as a function of HD sessions missed, patient characteristics, and census region and time fixed effects. Model 2 (Equation 3-2) changed the dependent variable to the log transformation of CR costs. Model 3 (Equation 3-3) added facility characteristics on top of the covariates used in Model 1. The dependent variable for Model 4 (Equation 3-4) is log (CR costs), and the covariates included are HD sessions missed, patient characteristics, facility characteristics, and census region and time fixed effects. For the regression analysis, each facility-year observation was weighted by the total number of dialysis sessions provided by the facility.

Equation 3-1 $$CR\,costs_{it} = \alpha_0 + \alpha_1 NA_{it} + \alpha_2 X_{it} + \mu_i + \nu_t + \varepsilon_{it}$$

Equation 3-2 $$\log(CR\,costs_{it}) = \beta_0 + \beta_1 NA_{it} + \beta_2 X_{it} + \mu_i + \nu_t + e_{it}$$

Equation 3-3 $$CR\,costs_{it} = \gamma_0 + \gamma_1 NA_{it} + \gamma_2 X_{it} + \gamma_3 FAC_{it} + \mu_i + \nu_t + \eta_{it}$$

Equation 3-4 $$\log(CR\,costs_{it}) = \theta_0 + \theta_1 NA_{it} + \theta_2 X_{it} + \theta_3 FAC_{it} + \mu_i + \nu_t + \sigma_{it}$$

$CR\cos ts_{it}$ is the composite rate costs per patient per month for dialysis facility *i* in year *t*. $\log(CR\cos ts_{it})$ is the log transformation of CR costs for facility *i* in year *t*. NA_{it} is the non-adherence measure representing the average HD sessions missed per patient per month for dialysis facility *i* in year *t*. X_{it} is a vector of patient characteristics for dialysis facility *i* in year *t*. FAC_{it} is the vector of facility characteristics for dialysis facility *i* in year *t*. The Census region (μ_i) and year (ν_t) dummy variables are also included to control for regional fixed effects and time trends. Finally, Huber robust standard error are reported to adjust for the heteroscedasticity in error terms among dialysis facilities.

Results

Descriptive analysis

Although the data show a certain degree of right-skewness in CR costs per month (Figure 3-1), it is not as pronounced as that found in the separately billable Medicare Allowable Payments (SB MAP) per month. After taking a log transformation in CR costs per month, we re-examined the shape of the distribution for log (CR costs). The shape more closely resembles to a bell-shaped distribution (Figure 3-2).

Summary statistics for all variables used in this study are presented (Table 3-1). There are two dependent variables used in this study. The average CR costs per patient per month from 2004-2006 is $2,089.50 (SD = $2,096.75). The log (CR costs) is 7.61 (SD = 0.20). The average HD sessions missed per patient per month, the independent

variable of interest, is 0.11 (SD = 0.078). In terms of demographics, the majority of HD patients in this study are between the ages of 45 and 79 (73.7 percent), males (53.3 percent), and White (54.1 percent).

There are several other important patient characteristics that were used in the regression models. The average body surface area (BSA) using a Dubois formula ($BSA(m^2) = 0.20247 \times Height(m)^{0.725} \times Weight(kg)^{0.425}$) is 1.87 per 0.1 m^2 (SD = 0.056). About 28 percent of the study population is underweight, which is defined by having a body mass index (BMI) less than 18.5. About 49 percent of HD patients have received dialysis treatments for more than three years. The most commonly observed comorbidities are diabetes (60 percent), peripheral vascular disease (45 percent), chronic obstructive pulmonary disease (28.3 percent), and cerebrovascular disease (26.1 percent). The least observed comorbidity is esophageal varices (0.04 percent).

For facility characteristics, 67 percent of the facility-year records indicated that more than 10,000 dialysis treatments were provided. About 70 percent of the records showed that dialysis treatments were provided by the six largest chains (Fresenius, Gambro, Davita, Renal Care Group, Dialysis Centers Inc, and National Nephrology Associates). Finally, 82 percent of these facility-year records are from urban location.

Regression analysis

Table 3-2 shows the set of estimated coefficients of the independent variables of interest on CR costs and log (CR costs), without the inclusion of facility characteristics. The coefficient estimate of non-adherence in Model 1 shows that if an HD session is missed

by a patient in one month, the CR costs per patient per month would increase by $462.61. However, this finding is not statistically significant. Statistically significant predictors on CR costs are the third year of renal replacement therapy, body surface area, and percent of HD patients with hepatitis B within one year.

For the log-linear model (Model 2), we found a statistically significant positive effect of non-adherence on log (CR costs). The coefficient estimate is 0.066, and after the retransformation to the unlogged scale, the multiplier derived from this estimate is 1.07. The interpretation for this multiplier is that if an HD session is missed by a patient in a month, the CR costs per patient per month would increase by 7 percentage points, which on a dollar scale is $146.27. Other statistically significant variables are older age, percentage of African American HD patients, start month and duration (3 years) of renal replacement therapy, body surface area, and 15 functional statuses and comorbid measures. The explanatory power, R-squared, is higher in the log-linear model (15.48 percent) than in the OLS model (1.59 percent).

Table 3-3 shows the regression results for the OLS and log-linear models, with the inclusion of facility characteristics. The coefficient estimate of non-adherence on CR costs is $284.66, which remains statistically insignificant. With the inclusion of facility characteristics, none of the patient characteristics has a statistically significant effect on measuring CR costs (Model 3). Unlike the findings from Model 2, the effect of non-adherence on log (CR costs) from Model 4 is not statistically significant after controlling for facility characteristics. Other statistically significant explanatory variables include age, sex, body surface area, low BMI, and 10 functional status and comorbid measures. The R-squared statistic increased slightly from 1.59 percent (in Model 1) to 3.37 percent

(in Model 3). The R-squared statistic increased considerably from 15.48 percent (in Model 2) to 39.44 percent (in Model 4), after the inclusion of facility characteristics.

Sensitivity analysis

We conducted a two-stage-least-square (2SLS) estimation on the association between CR costs and non-adherence, using distance and its square term as two instrumental variables. However, since the Hausman test rejected the existence of endogeneity at the facility level, the 2SLS results are not reported.

It is highly likely to observe more voluntary withdrawal cases for dialysis patients who are close to the end of life. Based on our identification strategy for non-adherence, we were not able to distinguish whether individual missed treatments were due to permanent withdrawal or temporary withdrawal. To address this concern of possible misclassification, we conducted a sensitivity analysis in which we dropped observations on the month of death and the month prior to death, to ensure the results are not biased.

After excluding the observations of "month of death" and "month prior to death," the sample size was reduced from 11,600 to 11,598 facility years (Table 3-4). For the OLS model without facility characteristics, the coefficient estimate on non-adherence dropped from $462.61 to $204.57, and remained statistically insignificant. The magnitude of coefficient estimates on other covariates dropped consistently, as compared with the original model. The coefficient estimate on non-adherence for the log-linear model is -0.0243 (multiplier=0.96), and is no longer statistically significant.

CR costs typically fluctuate more among dialysis patients who are close to the end of their lives. Results of this sensitivity analysis suggest that if we excluded these months with higher fluctuation in CR costs, the impact, in terms of magnitude, of non-adherence on CR costs is even smaller, and statistically insignificant for both linear and log-linear models.

For the OLS and log-linear models with the inclusion of facility characteristics, the results of this sensitivity analysis are somewhat different. For the OLS model, the coefficient estimate on non-adherence dropped to $46 (SD=$230) from $284.66 (SD=$608), and is again statistically insignificant. Most of the coefficient estimates on patient characteristics are smaller in scale, and are, not surprisingly, statistically insignificant. On the contrary, many of the coefficient estimates on facility characteristics increase after excluding records, suggesting that dialysis patients consumed higher CR services before they reached the end of life.

As a third sensitivity analysis, we excluded those months with any kind of "event" (e.g., hospitalization, withdrawal, death) being identified and re-fit all four models. The rationale to exclude these months is based on the fact that they have a zero probability of being identified as missing, according to the way we defined the non-adherence measure. Although in reality, a patient could plausibly have an "event" and also skipped an HD session in a particular month. In order to carefully examine the true effect of missing sessions on CR costs, it is important to see how sensitive the coefficient estimates are when excluding these "event" months. Table 3-5 shows the results. 11,584 facility years were used in this analysis. For both OLS models, with and without facility characteristics, the coefficient estimates on non-adherence are not statistically significant,

consistent with previous findings. For the log-linear models, the coefficient estimates on non-adherence increase for both models.

Discussion

This study makes several contributions to the ESRD non-adherence literature. First, although abundant studies had explored the effect of non-adherence on health outcomes and quality of life, none specifically looked at the impact of non-adherence of HD sessions in CR costs for dialysis providers. With the use of CMS Evidence Form (Form 2728) and claims files for all Medicare HD patients, we can estimate the impact of non-adherence on CR costs more accurately.

This study provides information on whether non-adherence in HD sessions is associated with cost-saving (or cost-increasing) for the providers, using CR costs as the health care costs measure. The findings from Model 1, Model 3, and Model 4 consistently show that there is no association between non-adherence and CR costs.

According to the log-linear model without controlling for facility characteristics (Model 2), non-adherence is associated with a seven percent increase (or $146.27) in CR costs. One possible explanation for the seven percent increase in CR costs in Model 2 is that the non-adherence measure picks up on the impact of those facility characteristics, e.g., hospital-based facilities, small and medium facility size, and regional chain status. All of these have a positive statistically significant impact on CR costs. When adding facility characteristics into the log-linear model (Model 4), the effect of non-adherence on CR costs fades away, suggesting that there are correlations between the average HD

sessions missed per patient per month and some or all of these facility characteristics.

Second, to take into account for the skewedness in CR costs, we examined both the linear and logarithmic forms of the case-mix models. Despite the exclusion and inclusion of facility characteristics, the explanatory power of the logarithmic models (Model 2 and Model 4) was higher than that of the linear models (Model 1 and Model 3). In addition, standard deviations derived from the logarithmic models consistently present a tighter distribution than those derived from OLS models. The findings suggest that the logarithmic form of CR costs model might be better than the linear form in satisfying the normality assumption of a statistical model. Logged estimates for health care costs are often more precise and robust than the direct analysis of unlogged dependent variables. However, researchers are not interested in log scale results due to the difficulty in interpreting the coefficient estimates in log dollars. When retransforming the logged estimates to the raw scale, Manning and colleagues (2001) suggested that researchers should consider a smearing adjustment (Duan, 1983) to correct for any form of heteroscedasticity in error terms to yield consistent predictions. We have not dealt with this concern in this study, and would like to revisit more about this retransformation issue in future research.

With the presence of non-adherence, total revenues for dialysis facilities are expected to drop due to fewer sessions provided. The study results show that there are no meaningful cost savings for dialysis facilities when patients skipped routine HD treatments. Consequently, there is a financial incentive for dialysis facilities to improve patient adherence in order to maximize profit. Dialysis facilities could consider using

various approaches, e.g., reminder phone calls, text messages, and e-mails, to target patients who are more likely to skip sessions to improve adherence.

From the perspective of the CMS, policy intervention to improve patient adherence seems unnecessary because the financial incentive associated with higher adherence is sufficient for dialysis facilities to monitor and improve adherence. From the societal perspective, assuming that dialysis facilities will internalize the costs associated with improving adherence without having incentive programs from the CMS, e.g. a pay-for-performance program, society as a whole would benefit from an increasing adherence in dialysis sessions, given that higher adherence is associated with better quality of life and better health outcomes from previous literature.

There are several limitations pertaining to this study. One limitation is related to the quality of Medicare cost report data. Researchers have raised concerns about the incompleteness of cost report data (Bednar, 1992; Magnus et al., 2000; Medicare Payment Advisory Commission, 2004). Being the only available data source of dialysis costs, cost reports have been used extensively. To the extent that the CMS has recently refined the minimum file requirements and increased the controls to monitor providers' behavior in "Potential Rejection Error," e.g., zero or negative values for the number of dialysis treatments, this concern is lessened. It is important to note that non-adherence, as defined in this study, is measured conservatively. For instance, if a patient is identified to have an event (e.g., hospitalization) in a month, then he will not be defined as a "missed" patient for that month based on our identification strategy. In reality, he might be both "hospitalized" and "non-adherent" for that month. For months with 31 days, patients may receive 13 treatments instead of 12 treatments. Suppose a record shows that

a patient received 11 treatments in a 31-day month, without any other event being identified. Using our identification strategy, this patient would be reported as missing one treatment, although in reality he missed two treatments. To the extent that this non-adherence measure was underestimated, the prevalence of non-adherence should be greater than 0.11 sessions per patient per month, and the coefficient estimates on non-adherence as well as other covariates could also be affected.

Figure 3-1. Distribution of CR costs per patient per month

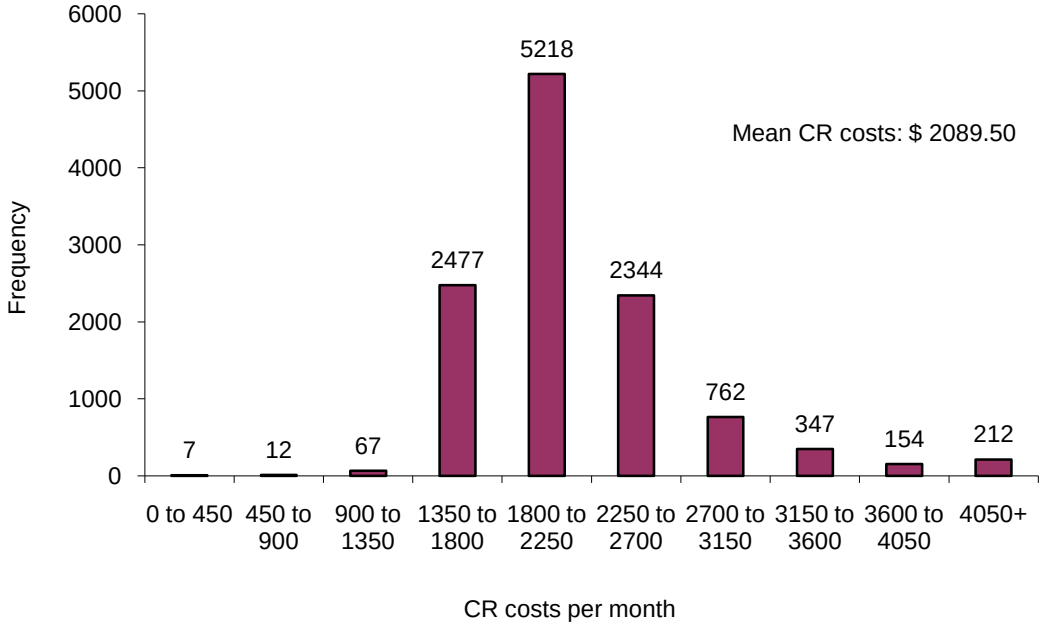

Figure 3-2. Distribution of log (CR costs per patient per month)

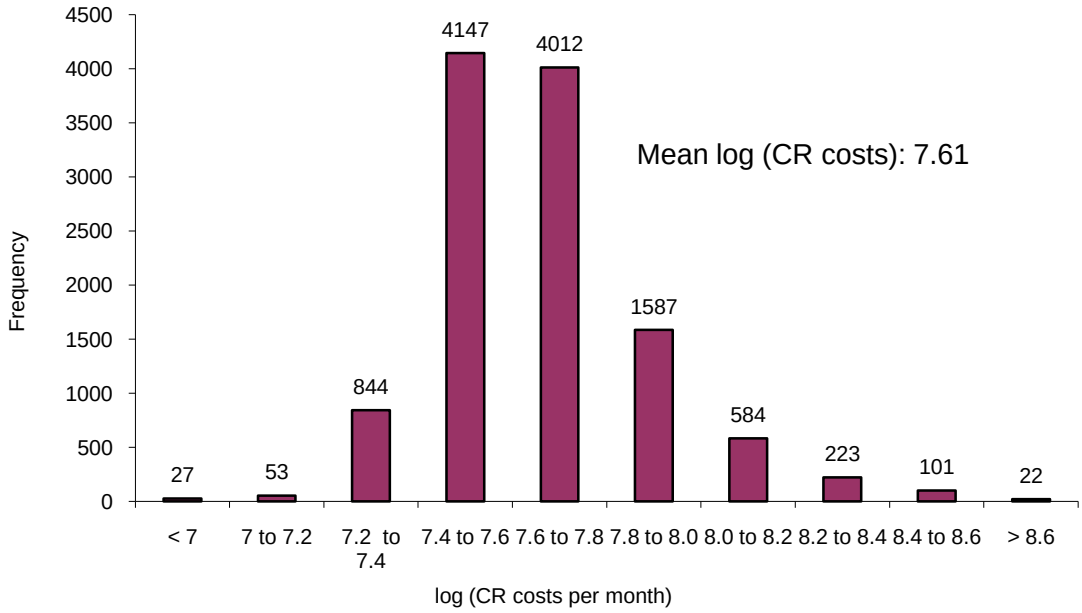

Table 3-1. Summary statistics of all variables, 2004-2006

Variables	Mean	S.D.
Dependent variables		
CR costs per month	2089.50	2096.75
log (CR costs per month)	7.61	0.20
Variable of interest		
Average HD sessions missed per patient per month	0.11	0.078
Demographic variables		
Ages <18 yrs	0.001	0.015
Ages 18-44 yrs	0.129	0.061
Ages 45-59 yrs	0.259	0.085
Ages 60-69 yrs	0.235	0.061
Ages 70-79 yrs	0.243	0.078
Ages 80+ yrs	0.133	0.077
Female	0.467	0.076
Race: Native American	0.016	0.077
Race: Asian	0.035	0.091
Race: Black	0.397	0.313
Race: White	0.541	0.302
Race: Other	0.011	0.023
Race: Unknown/missing	0.0002	0.0016
Patient characteristics and comorbidities		
Body surface area (Dubois formula)	1.867	0.056
Underweight (BMI <18.5 kg/m^2)	27.76	1.32
Started RRT during month	0.0058	0.0043
1 previous month of RRT	0.0148	0.0084
2 previous months of RRT	0.0149	0.0079
3 previous months of RRT	0.0186	0.0082
4 previous months of RRT	0.0178	0.0075
5 previous months of RRT	0.0179	0.0073
6 previous months of RRT	0.0170	0.0069
7 previous months of RRT	0.0172	0.0068
8 previous months of RRT	0.0163	0.0064
9 previous months of RRT	0.0160	0.0062
10-12 previous months of RRT	0.0474	0.0172
2nd year of RRT	0.164	0.049
3rd year of RRT	0.138	0.041
3 years or more of RRT	0.49	0.11
Inability to ambulate (2728)	0.026	0.030
Inability to transfer (2728)	0.008	0.015
Smoking	0.034	0.042
Alcohol Dependence between 1999-2004	0.053	0.037
Drug Dependence between 1999-2004	0.042	0.030
Cardiac Arrest within one year	0.012	0.013
Cardiac dysrhythmia within one year	0.34	0.11
Ischemic heart disease within one year	0.51	0.12
Pericarditis within one year	0.011	0.013
Cerebrovascular disease within one year	0.261	0.078
Diabetes within one year	0.60	0.11

Peripheral vascular disease within one year	0.45	0.11
Chronic obstructive pulmonary disease within one year	0.283	0.093
Acquired immunodeficiency disease within one year	0.015	0.024
Human immnodeficiency virus within one year	0.012	0.023
Bacterial Pneumonia six months ago	0.0047	0.0046
Hepatitis B within one year	0.012	0.043
Other Hepatitis between 1999-2004	0.072	0.068
Opportunistic Infection six months ago	0.0012	0.0021
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.0022	0.0031
Septicemia within six months	0.035	0.030
Gastro-Intestinal (GI) Tract Bleeding six months ago	0.0035	0.0032
GI Ulcer - no hemorrhage within six months	0.0060	0.0054
Esophogeal Varices within six months	0.0004	0.0011
Acquired Hemolytic Anemias within one year	0.013	0.078
Hereditary Hemolytic Anemias between 1999-2004	0.018	0.023
Sickle-Cell Anemia between 1999-2004	0.004	0.011
Leukemia within one year	0.0043	0.0093
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.012	0.013
Lymphoma within two years	0.007	0.011
Metastatic Cancers within one year	0.013	0.015
Multiple Myeloma within one year	0.008	0.012
Breast, Prostate, Colorectal and Other Cancers within one year	0.080	0.040
Hyperparathyroidism within one year	0.10	0.17
Monoclonal Gammopathy within one year	0.0061	0.0099
Myelofibrosis within one year	0.005	0.012
Myelodysplastic Syndrome between 1999-2004	0.012	0.017
Facility characteristics		
Hospital-based facility	0.07	0.25
Facility size: < 5,000 treatments	0.08	0.27
Facility size: 5,000 - 9,999 treatments	0.26	0.44
Facility size: 10,000+ treatments	0.67	0.47
Large dialysis organization (chain1-chain6)	0.70	0.46
Regional chain	0.10	0.30
Independent	0.17	0.37
Unknown	0.03	0.17
CR exception (HD claims or CMS list)	0.07	0.26
Rural location	0.18	0.38
Metropolitan area	0.83	0.37
Micropolitan area	0.12	0.32
Not in micro or metro area	0.05	0.21
N(facility-years)	11,600	

Table 3-2. OLS and Log-linear regression results (without facility characteristics)

Dependent variable	CR costs/month	log (CR costs/month)	
	OLS (1)	Log-linear (2)	
Variables	Coeff.	Coeff.	Mult.
Average HD sessions skipped per patient per month	462.61	0.066*	1.07
	(599.23)	(0.032)	-
Percent of HD patients with ages <18 years old	2829.03*	1.18**	3.25
	(1136.88)	(0.13)	-
Percent of HD patients with ages between 18 and 44 years old	-349.02	0.059	1.06
	(422.71)	(0.046)	-
Percent of HD patients with ages between 70 and 79 years old	79.19	0.11**	1.12
	(281.55)	(0.037)	-
Percent of HD patients with ages greater than 80 years old	93.78	0.18**	1.20
	(704.52)	(0.043)	-
Percent of female HD patients	210.49	0.09**	1.09
	(324.34)	(0.03)	-
Percent of African American HD patients	-209.30**	-0.06**	0.94
	(53.67)	(0.01)	-
Started renal replacement therapy during month	13094	4.70**	109.95
	(10386)	(0.78)	-
Third year of renal replacement therapy	-554.25*	-0.13**	0.88
	(246.35)	(0.044)	-
Body surface area (Dubois formula)	1619.8**	0.48**	1.61
	(603.75)	(0.051)	-
Percent of HD patient with BMI < 18.5 kg/m^2	1076.1	0.002	1.00
	(992.29)	(0.077)	-
Percent of HD patients with inability to ambulate (2728)	1855.41	0.19*	1.21
	(1801.32)	(0.092)	-
Percent of HD patients with smoking habit	83.82	0.13*	1.14
	(300.97)	(0.055)	-
Percent of HD patients with drug dependence	34.28	0.24**	1.28
	(394.32)	(0.063)	-
Percent of HD patients with ischemic heart disease within one year	-423.67	-0.068*	0.93
	(387.47)	(0.027)	-
Percent of HD patients with cerebrovascular disease within one year	-382.29	-0.095*	0.91
	(378.67)	(0.033)	-
Percent of HD patients with peripheral vascular disease within one year	631.29	0.070**	1.07
	(387.34)	(0.027)	-
Percent of HD patients with acquired immunodeficiency disease within one year	512.68	0.43**	1.54
	(475.79)	(0.12)	-
Percent of HD patients with bacterial pneumonia within six months	28615	1.45*	4.26
	(18898)	(0.65)	-
Percent of HD patients with hepatitis B within one year	703.1**	0.28**	1.32
	(214.03)	(0.069)	-
Percent of HD patients with septicemia within six months	-749.59	-0.072	0.93
	(517.00)	(0.088)	-

Percent of HD patients with gastro-intestinal ulcer within six months	-1417.94	-0.42	0.66
	(3298.59)	(0.40)	-
Percent of HD patients with opportunistic infection within six months	18833	1.85*	6.36
	(12187)	(0.86)	-
Percent of HD patients with acquired hemolytic anemias within one year	312.74**	0.17**	1.18
	(65.91)	(0.024)	-
Percent of HD patients with sickle-cell anemia	986.94	0.60**	1.82
	(656.89)	(0.14)	-
Percent of HD patients with hyperparathyroidism within one year	116.44	0.076**	1.08
	(65.55)	(0.015)	-
Percent of HD patients with myelofibrosis within one year	2533.57	0.57**	1.77
	(1494.83)	(0.15)	-
Percent of HD patients with myelodysplastic syndrome	-2157.50	-0.30**	0.74
	(1181.60)	(0.11)	-
Facility control variables	no	no	
Census region fixed effects	yes	yes	
Time trends	yes	yes	
R^2	1.59%	15.48%	
Observations	11,600	11,600	

Note: Huber Robust standard errors are in parentheses.

Fixed effects of census region and time trend are included in all specifications.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 37 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan area or not.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 3-3. OLS and Log-linear regression results (with facility characteristics)

Dependent variable	CR costs/month	log (CR costs/month)	
	OLS (3)	Log-linear (4)	
Variables	Coeff.	Coeff.	Mult.
Average HD sessions skipped per patient per month	284.66	0.016	1.02
	(608.00)	(0.027)	-
Percent of HD patients with ages <18 years old	937.83	0.50**	1.65
	(1147.39)	(.11)	-
Percent of HD patients with ages between 18 and 44 years old	-216.96	0.13**	1.14
	(443.44)	(0.038)	-
Percent of HD patients with ages between 70 and 79 years old	-42.63	0.075*	1.08
	(292.19)	(0.031)	-
Percent of HD patients with ages greater than 80 years old	-164.91	0.10**	1.11
	(712.92)	(0.035)	-
Percent of female HD patients	179.75	0.067**	1.07
	(315.62)	(0.023)	-
Percent of African American HD patients	-39.49	0.0021	1.00
	(41.19)	(0.0084)	-
Started renal replacement therapy during month	1008.16	0.33	1.39
	(10098)	(0.65)	-
Third year of renal replacement therapy	-392.48	-0.054	0.95
	(252.55)	(0.036)	-
Body surface area (Dubois formula)	987.4	0.22**	1.25
	(565.20)	(0.042)	-
Percent of HD patient with BMI < 18.5 kg/m^2	687.62	-0.13*	0.88
	(935.79)	(0.065)	-
Percent of HD patients with inability to ambulate (2728)	1061.19	-0.062	0.94
	(1713.61)	(0.077)	-
Percent of HD patients with smoking habit	-228.44	-0.009	0.99
	(266.53)	(0.047)	-
Percent of HD patients with drug dependence	-219.29	0.18*	1.19
	(438.98)	(0.055)	-
Percent of HD patients with ischemic heart disease within one year	-374.97	-0.048*	0.95
	(384.28)	(0.022)	-
Percent of HD patients with cerebrovascular disease within one year	-178.66	-0.009	0.99
	(374.35)	(0.028)	-
Percent of HD patients with peripheral vascular disease within one year	594.85	0.077**	1.08
	(351.91)	(0.022)	-
Percent of HD patients with acquired immunodeficiency disease within one year	168.08	0.32**	1.38
	(463.81)	(0.09)	-
Percent of HD patients with bacterial pneumonia within six months	27040	0.83	2.29
	(18808)	(0.6)	-
Percent of HD patients with hepatitis B within one year	286.02	0.12*	1.13
	(193.68)	(0.049)	-
Percent of HD patients with septicemia within six months	-1157.56	-0.18*	0.83
	(601.45)	(0.075)	-

Percent of HD patients with gastro-intestinal ulcer within six months	-4358.79	-1.50**	0.22
	(3258.64)	(0.37)	-
Percent of HD patients with opportunistic infection within six months	17095	0.99	2.69
	(12411)	(0.74)	-
Percent of HD patients with acquired hemolytic anemias within one year	149.87	0.13**	1.14
	(100.48)	(0.022)	-
Percent of HD patients with sickle-cell anemia	732.69	0.58**	1.79
	(736.02)	(0.15)	-
Percent of HD patients with hyperparathyroidism within one year	-40.46	0.028*	1.03
	(76.87)	(0.012)	-
Percent of HD patients with myelofibrosis within one year	1387.37	0.11	1.12
	(1525.65)	(0.12)	-
Percent of HD patients with myelodysplastic syndrome	-1374.11	-0.012	0.99
	(1114.02)	(0.093)	-
Hospital-based facility	818.43**	0.34**	1.40
	(72.99)	(0.015)	-
Facility size: < 5,000 treatments	807.59**	0.23**	1.26
	(195.64)	(0.008)	-
Facility size: 5,000 - 9,999 treatments	224.92**	0.10**	1.11
	(9.70)	(0.003)	-
Large dialysis organization (chain1-chain6)	-56.30	0.021**	1.02
	(91.90)	(0.006)	-
Regional chain	59.43	0.030**	1.03
	(139.81)	(0.009)	-
Unknown	45.22	0.041*	1.04
	(61.50)	(0.021)	-
CR exception (HD claims or CMS list)	48.61*	0.029**	1.03
	(21.03)	(0.007)	-
Rural location	-128.21*	-0.034	0.97
	(63.75)	(0.02)	-
Metropolitan area	-53.79	-0.041*	0.96
	(59.84)	(0.021)	-
Not in micro or metro area	-50.36	0.006	1.01
	(44.82)	(0.007)	-
Facility control variables	yes	yes	
Census region fixed effects	yes	yes	
Time trends	yes	yes	
R^2	3.37%	39.44%	
Observations	11,600	11,600	

Note: Huber Robust standard errors are in parentheses.

Fixed effects of census region and time trend are included in all specifications.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 37 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan area or not.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 3-4. First sensitivity analysis: OLS and Log-linear regression results after the exclusion of month of death and the month prior to death (without facility characteristics)

Dependent variable	CR costs/month	log (CR costs/month)	
	OLS (1)	Log-linear (2)	
Variables	Coeff.	Coeff.	Mult.
Percent of HD sessions skipped in the month	204.57	-0.024	0.98
	(439.42)	(0.033)	-
Percent of HD patients with ages <18 years old	1899.37	0.85**	2.35
	(1219.05)	(0.10)	-
Percent of HD patients with ages between 18 and 44 years old	-93.18	0.14*	1.15
	(515.88)	(0.058)	-
Percent of HD patients with ages between 70 and 79 years old	-16.31	0.075	1.08
	(281.71)	(0.041)	-
Percent of HD patients with ages greater than 80 years old	-6.35	0.12*	1.13
	(639.29)	(0.046)	-
Percent of female HD patients	70.89	0.035	1.04
	(334.64)	(0.032)	-
Percent of African American HD patients	-229.27**	-0.055	0.95
	(70.70)	(0.012)	-
Started renal replacement therapy during month	9496.7	2.8*	16.44
	(7186.72)	(1.30)	-
Third year of renal replacement therapy	-395.88	-0.045	0.96
	(357.17)	(0.056)	-
Body surface area (Dubois formula)	1508.86*	0.37**	1.45
	(612.73)	(0.056)	-
Percent of HD patient with BMI < 18.5 kg/m^2	1290.31	-0.013	0.99
	(1269.20)	(0.10)	-
Percent of HD patients with inability to ambulate (2728)	1984.69	0.1	1.11
	(2217.92)	(0.10)	-
Percent of HD patients with smoking habit	21.3	0.14*	1.15
	(351.78)	(0.062)	-
Percent of HD patients with drug dependence	151.09	0.26**	1.29
	(371.39)	(0.076)	-
Percent of HD patients with ischemic heart disease within one year	-432.45	-0.057	0.94
	(437.11)	(0.032)	-
Percent of HD patients with cerebrovascular disease within one year	-289.54	-0.085*	0.92
	(462.98)	(0.043)	-
Percent of HD patients with peripheral vascular disease within one year	800.47	0.1**	1.11
	(470.76)	(0.03)	-
Percent of HD patients with acquired immunodeficiency disease within one year	282.12	0.3*	1.35
	(529.61)	(0.14)	-
Percent of HD patients with bacterial pneumonia within six months	24458	0.7	2.01
	(16450)	(0.90)	-
Percent of HD patients with hepatitis B within one year	507.25*	0.19**	1.21
	(248.07)	(0.069)	-
Percent of HD patients with septicemia within six months	-882.30	-0.035	0.97

	(715.83)	(0.09)	-
Percent of HD patients with gastro-intestinal ulcer within six months	1101.2	0.33	1.39
	(3540.42)	(0.48)	-
Percent of HD patients with opportunistic infection within six months	15110	0.02	1.02
	(13230)	(0.83)	-
Percent of HD patients with acquired hemolytic anemias within one year	198.45*	0.13**	1.13
	(84.47)	(0.025)	-
Percent of HD patients with sickle-cell anemia	1291.29	0.67**	1.95
	(867.05)	(0.22)	-
Percent of HD patients with hyperparathyroidism within one year	83.06	0.069**	1.07
	(72.36)	(0.014)	-
Percent of HD patients with myelofibrosis within one year	2562.04	0.33	1.39
	(2167.21)	(0.19)	-
Percent of HD patients with myelodysplastic syndrome	-2595.33	-0.04	0.96
	(2074.09)	(0.15)	-
Facility control variables	no	no	
Census region fixed effects	yes	yes	
Time trends	yes	yes	
R^2	1.49%	13.23%	
Observations	11,598	11,598	

Note: Huber Robust standard errors are in parentheses.

Fixed effects of census region and time trend are included in all specifications.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 37 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan area or not.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 3-4. First sensitivity analysis: OLS and Log-linear regression results after the exclusion of month of death and the month prior to death (with facility characteristics)

Dependent variable	CR costs/month	log (CR costs/month)	
	OLS (3)	Log-linear (4)	
Variables	Coeff.	Coeff.	Mult.
Percent of HD sessions skipped in the month	46	-0.066*	0.94
	(437.76)	(0.027)	-
Percent of HD patients with ages <18 years old	347.38	0.33**	1.39
	(1243.63)	(0.093)	-
Percent of HD patients with ages between 18 and 44 years old	-164.46	0.15**	1.16
	(557.73)	(0.048)	-
Percent of HD patients with ages between 70 and 79 years old	-157.84	0.04	1.04
	(293.37)	(0.034)	-
Percent of HD patients with ages greater than 80 years old	-320.88	0.036	1.04
	(649.55)	(0.04)	-
Percent of female HD patients	58.84	0.019	1.02
	(317.22)	(0.026)	-
Percent of African American HD patients	-27.98	0.02*	1.02
	(60.94)	(0.01)	-
Started renal replacement therapy during month	615.42	-0.23	0.79
	(6351.84)	(0.83)	-
Third year of renal replacement therapy	-240.60	0.017	1.02
	(355.80)	(0.047)	-
Body surface area (Dubois formula)	943.31	0.15**	1.16
	(571.60)	(0.047)	-
Percent of HD patient with BMI < 18.5 kg/m^2	910.56	-0.15	0.86
	(1250.22)	(0.085)	-
Percent of HD patients with inability to ambulate (2728)	1226.4	-0.14	0.87
	(2146.09)	(0.088)	-
Percent of HD patients with smoking habit	-296.15	-0.023	0.98
	(283.71)	(0.052)	-
Percent of HD patients with drug dependence	-151.77	0.18**	1.20
	(426.50)	(0.063)	-
Percent of HD patients with ischemic heart disease within one year	-341.53	-0.019	0.98
	(434.80)	(0.027)	-
Percent of HD patients with cerebrovascular disease within one year	-250.29	-0.056	0.95
	(453.05)	(0.039)	-
Percent of HD patients with peripheral vascular disease within one year	690.98	0.084**	1.09
	(427.07)	(0.026)	-
Percent of HD patients with acquired immunodeficiency disease within one year	31.94	0.24*	1.27
	(494.42)	(0.11)	-
Percent of HD patients with bacterial pneumonia within six months	22577	0.01	1.01
	(16423)	(0.88)	-
Percent of HD patients with hepatitis B within one year	154.74	0.08	1.08
	(249.90)	(0.055)	-

Percent of HD patients with septicemia within six months	-1456.94	-0.18*	0.83
	(843.13)	(0.078)	-
Percent of HD patients with gastro-intestinal ulcer within six months	-1248.83	-0.54	0.58
	(3462.15)	(0.45)	-
Percent of HD patients with opportunistic infection within six months	14859	-0.21	0.81
	(13621)	(0.77)	-
Percent of HD patients with acquired hemolytic anemias within one year	-5.09	0.094**	1.10
	(146.77)	(0.023)	-
Percent of HD patients with sickle-cell anemia	795.31	0.53**	1.70
	(850.53)	(0.19)	-
Percent of HD patients with hyperparathyroidism within one year	-80.22	0.025*	1.03
	(90.92)	(0.012)	-
Percent of HD patients with myelofibrosis within one year	1627.7	-0.02	0.98
	(2195.48)	(0.16)	-
Percent of HD patients with myelodysplastic syndrome	-2201.60	0.09	1.09
	(2029.89)	(0.12)	-
Hospital-based facility	764.8**	0.32**	1.37
	(101.55)	(0.014)	-
Facility size: < 5,000 treatments	816.46**	0.27**	1.30
	(115.54)	(0.007)	-
Facility size: 5,000 - 9,999 treatments	239.18**	0.11**	1.11
	(10.12)	(0.004)	-
Large dialysis organization (chain1-chain6)	-86.64	0.032**	1.03
	(137.55)	(0.007)	-
Regional chain	73.91	0.038**	1.04
	(200.63)	(0.009)	-
Unknown	229.69*	0.097**	1.10
	(94.90)	(0.021)	-
CR exception (HD claims or CMS list)	59.35**	0.031**	1.03
	(22.25)	(0.008)	-
Rural location	-162.66**	-0.041**	0.96
	(62.60)	(0.014)	-
Metropolitan area	-38.19	-0.045**	0.96
	(63.88)	(0.015)	-
Not in micro or metro area	-56	-0.002	1.00
	(40.23)	(0.008)	-
Facility control variables	yes	yes	
Census region fixed effects	yes	yes	
Time trends	yes	yes	
R^2	3.16%	37.76%	
Observations	11,598	11,598	

Note: Huber Robust standard errors are in parentheses.

Fixed effects of census region and time trend are included in all specifications.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 37 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan area or not.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 3-5. Second sensitivity analysis: OLS and Log-linear regression results after the exclusion of months of any type of events (without facility characteristics)

Dependent variable	CR costs/month	log (CR costs/month)	
	OLS (1)	Log-linear (2)	
Variables	Coeff.	Coeff.	Mult.
Percent of HD sessions skipped in the month	-53.84	0.10**	1.11
	(108.23)	(0.021)	-
Percent of HD patients with ages <18 years old	170.92*	0.87**	2.38
	(75.18)	(0.092)	-
Percent of HD patients with ages between 18 and 44 years old	-1.91	0.15**	1.17
	(38.93)	(0.059)	-
Percent of HD patients with ages between 70 and 79 years old	-2.73	0.08	1.08
	(22.89)	(0.041)	-
Percent of HD patients with ages greater than 80 years old	7.95	0.13**	1.14
	(45.54)	(0.046)	-
Percent of female HD patients	1.96	0.02	1.02
	(20.66)	(0.032)	-
Percent of African American HD patients	-13.58*	-0.031*	0.97
	(5.33)	(0.014)	-
Started renal replacement therapy during month	320.28	1.54**	4.66
	(178.23)	(0.54)	-
Third year of renal replacement therapy	-23.40	-0.043	0.96
	(23.08)	(0.054)	-
Body surface area (Dubois formula)	105.16*	0.32**	1.38
	(49.08)	(0.056)	-
Percent of HD patient with BMI < 18.5 kg/m^2	81.06	0.003	1.00
	(71.33)	(0.097)	-
Percent of HD patients with inability to ambulate (2728)	170.01	0.1	1.11
	(190.66)	(0.10)	-
Percent of HD patients with smoking habit	-4.09	0.089	1.09
	(23.78)	(0.062)	-
Percent of HD patients with drug dependence	37.97	0.33**	1.40
	(33.62)	(0.086)	-
Percent of HD patients with ischemic heart disease within one year	-34.56	-0.044	0.96
	(37.30)	(0.033)	-
Percent of HD patients with cerebrovascular disease within one year	-2.79	-0.046	0.96
	(42.30)	(0.054)	-
Percent of HD patients with peripheral vascular disease within one year	70.51	0.11**	1.12
	(41.54)	(0.03)	-
Percent of HD patients with acquired immunodeficiency disease within one year	59.69	0.35	1.42
	(54.78)	(0.18)	-
Percent of HD patients with bacterial pneumonia within six months	1076.24	0.42	1.52
	(749.72)	(0.60)	-
Percent of HD patients with hepatitis B within one year	48.58*	0.19*	1.21
	(21.52)	(0.075)	-
Percent of HD patients with septicemia within six months	-41.10	0.085	1.09

	(59.01)	(0.091)	-
Percent of HD patients with gastro-intestinal ulcer within six months	69.03	0..25	1.28
	(136.03)	(0.45)	-
Percent of HD patients with opportunistic infection within six months	342.7	3.84	46.53
	(178.32)	(2.85)	-
Percent of HD patients with acquired hemolytic anemias within one year	20.47**	0.14**	1.15
	(6.90)	(0.027)	-
Percent of HD patients with sickle-cell anemia	91.17	0.63**	1.88
	(78.16)	(0.24)	-
Percent of HD patients with hyperparathyroidism within one year	7.75	0.071**	1.07
	(5.92)	(0.014)	-
Percent of HD patients with myelofibrosis within one year	131.77	0.36*	1.43
	(126.42)	(0.17)	-
Percent of HD patients with myelodysplastic syndrome	-51.85	0.21	1.23
	(98.49)	(0.16)	-
Facility control variables	no	no	
Census region fixed effects	yes	yes	
Time trends	yes	yes	
R^2	1.46%	15.26%	
Observations	11,584	11,584	

Note: Huber Robust standard errors are in parentheses.

Fixed effects of census region and time trend are included in all specifications.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 37 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan area or not.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

Table 3-5. Second sensitivity analysis: OLS and Log-linear regression results after the exclusion of months of any type of events (with facility characteristics)

Dependent variable	CR costs/month	log (CR costs/month)	
	OLS (3)	Log-linear (4)	
Variables	Coeff.	Coeff.	Mult.
Percent of HD sessions skipped in the month	24.2	0.065**	1.07
	(101.85)	(0.016)	-
Percent of HD patients with ages <18 years old	35.16	0.31**	1.37
	(78.60)	(0.083)	-
Percent of HD patients with ages between 18 and 44 years old	-9.36	0.16**	1.17
	(41.63)	(0.048)	-
Percent of HD patients with ages between 70 and 79 years old	-16.28	0.037	1.04
	(23.92)	(0.034)	-
Percent of HD patients with ages greater than 80 years old	-18.88	0.046	1.05
	(45.73)	(0.037)	-
Percent of female HD patients	0.7	0.002	1.00
	(19.34)	(0.025)	-
Percent of African American HD patients	3.63	0.048**	1.05
	(4.55)	(0.012)	-
Started renal replacement therapy during month	146.05	0.74*	2.10
	(146.65)	(0.37)	-
Third year of renal replacement therapy	-11.35	0.016	1.02
	(22.45)	(0.043)	-
Body surface area (Dubois formula)	62.17	0.12**	1.12
	(45.40)	(0.045)	-
Percent of HD patient with BMI < 18.5 kg/m^2	49.39	-0.13	0.88
	(68.01)	(0.081)	-
Percent of HD patients with inability to ambulate (2728)	112.56	-0.12	0.89
	(184.92)	(0.092)	-
Percent of HD patients with smoking habit	-26.70	-0.058	0.94
	(18.62)	(0.051)	-
Percent of HD patients with drug dependence	4.95	0.23**	1.26
	(35.21)	(0.064)	-
Percent of HD patients with ischemic heart disease within one year	-25.65	-0.0004	1.00
	(36.88)	(0.028)	-
Percent of HD patients with cerebrovascular disease within one year	-4.41	-0.039	0.96
	(41.11)	(0.054)	-
Percent of HD patients with peripheral vascular disease within one year	60.79	0.087**	1.09
	(38.04)	(0.025)	-
Percent of HD patients with acquired immunodeficiency disease within one year	31.15	0.26	1.30
	(46.91)	(0.14)	-
Percent of HD patients with bacterial pneumonia within six months	958.03	-0.12	0.89
	(744.12)	(0.48)	-
Percent of HD patients with hepatitis B within one year	15.54	0.058	1.06
	(20.83)	(0.063)	-
Percent of HD patients with septicemia within six months	-96.86	-0.092	0.91

	(70.09)	(0.075)	-
Percent of HD patients with gastro-intestinal ulcer within six months	-111.63	-0.54	0.58
	(128.14)	(0.41)	-
Percent of HD patients with opportunistic infection within six months	291.86	0.55**	1.73
	(184.89)	(0.087)	-
Percent of HD patients with acquired hemolytic anemias within one year	3.21	0.11**	1.12
	(11.71)	(0.024)	-
Percent of HD patients with sickle-cell anemia	73.66	0.58**	1.79
	(72.39)	(0.21)	-
Percent of HD patients with hyperparathyroidism within one year	-6.20	0.026*	1.03
	(7.54)	(0.012)	-
Percent of HD patients with myelofibrosis within one year	61.98	0.03	1.03
	(126.55)	(0.13)	-
Percent of HD patients with myelodysplastic syndrome	-62.85	0.147	1.16
	(91.48)	(0.096)	-
Hospital-based facility	66.71**	0.33**	1.39
	(7.69)	(0.014)	-
Facility size: < 5,000 treatments	72.02**	0.29**	1.33
	(10.25)	(0.007)	-
Facility size: 5,000 - 9,999 treatments	20.80**	0.11**	1.12
	(0.86)	(0.004)	-
Large dialysis organization (chain1-chain6)	-6.14	0.034**	1.03
	(10.80)	(0.007)	-
Regional chain	6.43	0.033**	1.03
	(16.13)	(0.009)	-
Unknown	20.65**	0.098**	1.10
	(7.05)	(0.022)	-
CR exception (HD claims or CMS list)	5.44**	0.031**	1.03
	(1.88)	(0.007)	-
Rural location	-14.89*	-0.04**	0.96
	(5.90)	(0.014)	-
Metropolitan area	-2.16	-0.035*	0.97
	(4.51)	(0.015)	-
Not in micro or metro area	-4.93	-0.004	1.00
	(3.17)	(0.008)	-
Facility control variables	yes	yes	
Census region fixed effects	yes	yes	
Time trends	yes	yes	
R^2	3.37%	41.07%	
Observations	11,584	11,584	

Note: Huber Robust standard errors are in parentheses.

Fixed effects of census region and time trend are included in all specifications.

The exogenous variables included in all models are age, female, race, duration of RRT, body surface area, low BMI, 37 functional and comorbid conditions, hospital-based or freestanding facilities, facility size, chain status, exception, rural/urban location, and metropolitan area or not.

* Significantly different from zero at 95 percent confidence.

** Significantly different from zero at 99 percent confidence.

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Chapter IV

Chapter IV. Is Non-adherence in Hemodialysis a Contributing Factor to Kidney Transplantation Failure?

Abstract

Using broad population data and a robust statistical approach, I did not consistently find a link between non-adherence in hemodialysis (HD) sessions, which was measured pre-transplant, and kidney transplantation failure. Although in a sensitivity analysis in which months with any kind of events were excluded (e.g., hospitalization and withdrawal), I did observe an association between a binary non-adherence measure and kidney transplantation failure. Data were analyzed using twelve Cox proportional hazards models, controlling for patient case-mix adjusters. These include patient demographics such as age and race, duration of renal replacement therapy (RRT), body surface area, BMI<18.5 kg/m^2, functional statuses, and clinical comorbidities. Results are consistent across these statistical models, indicating that there is no statistically significant relationship between non-adherence in hemodialysis sessions and kidney transplantation failure.

Though this association has been explored in the end-stage renal disease (ESRD) transplantation literature, population-based information has not yet been formed due to

limited data sources from previous studies. This observational study uses 18,393 kidney transplant recipients from 2004 to 2006. Data sources are from the CMS Medical Evidence Form (CMS Form 2728) and Medicare claims. A different perspective is given using average skipped HD sessions as the measure for non-adherence, instead of using the intake of immunosuppressive drugs.

Previous studies consistently found an association between non-adherence in medication regime and kidney transplantation failure. They emphasized the importance of design schemes in improving patients' adherence to medication. Findings from this study suggest that implementing an intervention to improve non-adherence in hemodialysis sessions in order to decrease the likelihood of kidney transplantation failure may not be cost-effective, since no causality between non-adherence in HD sessions and kidney transplantation failure was established.

Key words. Non-adherence, hemodialysis, kidney transplantation, kidney transplantation failure, Cox proportional hazards model

Introduction

Because it takes discipline and determination for dialysis patients to adhere to three routine dialysis sessions per week, and six to ten medications per day (Loghman-Adham, 2003), non-adherence in hemodialysis sessions is an important research topic in the end-stage renal disease (ESRD) literature. Previous research has demonstrated that kidney transplantation is a better form of treatment for ESRD patients because, compared to

dialysis patients, kidney transplant recipients live longer, enjoy better quality of life, and use fewer health care resources (Wolfe et al., 1999; Laupacis et al., 1996; Winkelmayer et al, 2002; Gill et al., 2009). However, kidney transplant recipients need to adhere to the lifelong intake of immunosuppressive medication to prevent a progression towards kidney transplantation failure (Michelon et. al, 1999).

Though the average cost of a kidney transplant ranges widely between $25,000 and $150,000, the costs of dialysis treatments are consistently higher over time. Costs fluctuate depending on whether the kidney transplant recipient has a deceased or living donor transplant. The severity of rejection and the number of medications or procedures needed after the transplantation also affect hospital costs. The costs for prescriptions for a recipient after being discharged ranges from between $700 to $2,000 per month (Emory health care website, 2009). From both a quality of life and health care costs perspective, a kidney transplantation failure is undesirable.

Literature Review

Non-adherence is an important research area in kidney transplantation literature because non-adherence is frequently observed among kidney transplant recipients. Adherence to medical regimens after a kidney transplantation is required to maintain good functional status of the transplanted kidney (Griffin et al., 2001). There is a wide variation in non-adherence rates as researchers use different measurements for time post-transplant and various definitions for non-adherence (Greenstein et al, 1999). The incidence of non-adherence after renal transplantation could be as high as 75 percent (Troppmann et al.,

1995). The range of kidney graft loss due to non-adherence is reported to be from 0.6 percent to 1.3 percent (Najarian 1975; Ettenger et al., 1991).

Several studies investigated the predictors for non-adherence post-transplant. Greenstein and colleagues (1999) identified that education, employment, and occupation are significant predictors of adherence. Kiley and colleagues (1993) found that there is an association between lower adherence rate and unemployment status. Sehweizer and colleagues concluded that patients with lower socioeconomic status have lower adherence. Other studies consistently found that younger patients have a higher incidence of non-adherence (Rovelli 1985; Lai 1992; Garcia 1997). Siegal and colleagues found that a longer interval after the transplant significantly increased the likelihood of non-adherence, plausibly because patients are less aware of their medication regimens. Previous studies have identified factors that might be associated with a higher risk of non-adherence. These predictors include age, sex, socioeconomic status, education level, complexity of treatment, duration or type of immunosuppressive regimens, patients' belief in treatment efficacy, and type of kidney donor (Rovelli et al., 1985; Lai et al., 1992; Schweizer et al., 1990; Didlake et al., 1998; Frazier et al., 1994; Garcia et al., 1999).

Many studies investigated the impact of non-adherence in medication regimen on kidney graft loss. Garcia and colleagues (1997) found a non-adherence incidence with graft loss of 3.4 percent. Michelon and colleagues (1999) found that the incidence of non-adherence leading to graft loss was different in relation to post-transplant time. The results from Morrissey and colleagues (2005) show that non-adherence is a risk factor for acute rejection, and acute rejection is a risk factor for allograft failure. Examining the

impact of non-adherence on outcome for pediatric kidney transplant recipients, Jarzembowski and colleagues (2004) found that there is a significant association between non-adherence and worse long-term graft survival in African American children.

Conceptual Framework

Several studies have investigated whether non-adherence is a major cause of kidney graft failure (Morrissey et al., 2005; Garcia et al., 1997; Michelon et al., 1999). These researchers consistently found that non-adherence, as defined by the irregular intake of immunosuppressive medication, is associated with late acute rejection. There are three limitations on the findings from these studies. First, these studies were limited by focusing on only one medical institution. This study uses Medicare data that include Medicare HD patients who received kidney transplantations across the nation.

Second, most of these studies used simple statistical methods which do not control for other exogenous variables. Previous research focused on descriptive statistics, univariate regression, simple correlations, Student's t test, chi-square test, and the Kaplan-Meier estimation. This study uses Cox proportional hazards models to predict kidney transplantation failure, which takes into account the interval until the first kidney transplantation and transplantation failure and controls for a full list of patient case-mix characteristics.

Third, the non-adherence of previous studies is measured by the quantity intake of the immunosuppressive regimen. This study used the average number of hemodialysis sessions skipped in a month. This new non-adherence measure is important in that

treatment types (hemodialysis, peritoneal, or kidney transplantation) for ESRD are sequential. Most kidney transplant recipients were on dialysis for a certain period of time until they could receive kidney transplantation. If there is an association between non-adherence in hemodialysis sessions and kidney transplantation failure, then this finding could possibly affect the kidney allocation score (KAS) system (Wolfe et al., 1999), or be used to target patients for counseling about adherence prior to transplant and for more aggressive monitoring or support after transplant. Dialysis patients with a higher adherence rate will have an allocation advantage for organs. I assume that dialysis patients are rational in their decision-making process on whether to adhere to dialysis protocols. If they are aware of this information that lower adherence will lead to a lower likelihood of receiving kidney transplantation, then we should be able to observe a spontaneous decrease in the non-adherence rate without any policy intervention. This would help dialysis outcomes but not necessarily post-transplant outcomes.

For the conceptual model, I would like to test whether non-adherence is a broad concept or a specific concept. I define "broad non-adherence" as non-adherence as a consistent behavior that carries across different types of medical treatment. For example, if a patient is non-adherent in receiving dialysis treatments pre-transplant, he likely will be non-adherent in taking immunosuppressant drugs, in keeping his medical appointments, and in following medical guidelines post transplantation. "Specific non-adherence" refers to a patient who is non-adherent in receiving dialysis treatments pre-transplant, yet would adhere to other medical treatments, such as taking immunosuppressant drugs, keeping medical appointments, and following medical

guidelines, post-transplant. Non-adherence in one aspect of life is independent of adherence to other medical treatments.

Under the "broad non-adherence" scenario, the benefit-cost structure of a patient's decision in being adherent is static pre- and post- transplant. The patient faces the question – How should I allocate my time to maximize utility? The utility is a measure of the satisfaction derived from the allocation of time used to receive dialysis treatments or used to do other activities. The patient must choose whether to adhere to routine dialysis treatments. The benefits of being adherent include longer life expectancy, positive feelings of control, and a sense of responsibility for others (family, friends). The costs of being adherent are: time costs (travel time for dialysis patients from home to dialysis facility), the physical and mental discomfort of treatment (injected syringes into their body for 3~4 hours per session), effort (three sessions per week), and the opportunity costs of not doing activities that interest them (socializing with friends and family, working). If a patient perceives the benefits of being adherent do not justify the costs, then he may skip routine sessions. Since non-adherence is a broad concept, these patients would also be non-adherent in taking immunosuppressant drugs post-transplantation, and thus have a higher risk of experiencing kidney transplantation failure. I would expect to see non-adherence in hemodialysis sessions having a positive effect on kidney transplantation failure.

Under the "specific non-adherence" scenario, I assume that a kidney transplantation is perceived by a patient as a critical event in life. His benefit-cost structure in deciding whether to be non-adherent shifts pre- and post-transplant. The benefit-cost structure is dynamic over time. A patient who is non-adherent in

hemodialysis sessions pre-transplant reconsiders his benefit-cost structure in being non-adherent post-transplant. He transforms to believe that long-term health benefits outweigh short-term leisure, and becomes more adherent to taking immunosuppressant drugs. I would expect to see a lower (or no) impact of non-adherence in hemodialysis on kidney transplantation failure.

Methods and Data

Methods

For the first part of this analysis, I use three Cox proportional hazards models to examine the effect of non-adherence in hemodialysis on the risk of having a kidney transplantation failure, after adjusting for none, some, and a full list of patient characteristics and comorbidities. For the second part of the study, I use a binary measure for non-adherence to estimate this association to check for non-linear effects.

3.1 Cox proportional hazards model

The Cox proportional hazards model is a statistical model used in survival analysis to demonstrate the multiplicative effect of several designated covariates, showing that this effect does not change over time.

Equation 4-1 $\lambda_i(t) = \lambda_0(t)\exp\{\beta^T Z_i\}$

In Equation 4-1, $\lambda_i(t)$ is the resultant hazard, $\lambda_0(t)$ is the baseline hazard, β is a vector of parameter estimates, T is duration, and Z_i is the vector of covariates. Model 1 estimated the hazard ratio of non-adherence on kidney transplantation failure without any patient case-mix adjusters. Model 2 added age, sex, race, time since start of renal replacement therapy, body surface area, and an underweight measure (BMI<18.5 kg/m^2). Model 3 further adjusted for 37 functional status and comorbid measures. Models 4 through 6 resembled models 1 through 3, except that I used a binary variable to define skipped sessions as the second non-adherence measure to test for non-linear effects.

Data

I used Standard Analytical Files (SAF) from the CMS to identify patient information with respect to kidney transplantation and kidney transplantation failure. Medicare claims for hemodialysis patients for whom Medicare was the primary payer between January 1, 2004, and December 31, 2006, were used and merged with SAF to derive the final study sample of 18,393 kidney transplantation recipients. Patient demographics, time since start of renal replacement therapy, functional status, and comorbidities were obtained from the CMS Medical Evidence Form (CMS Form 2728) and/or Medicare claims.

Variable

Dependent variable

The dependent variable is a binary variable coded "1" if a kidney transplantation recipient is identified to have a kidney transplantation failure and coded "0" if the transplantation is successful during this study period. Death is also coded as a failure event. A kidney transplantation recipient could have multiple kidney transplantations and thus multiple kidney transplantation failures. In this study, I only observe the kidney transplantation recipients until their first kidney transplantation failure occurred. I did not deal with multiple kidney transplantation failures in order to simplify my models and to make the interpretation cleaner.

Independent variable of interest

The independent variable of interest, non-adherence, is measured as the average number of HD sessions skipped in a month. The follow up days, a measure needed for the Cox proportional hazards model, was calculated as the difference in days between the date of first kidney transplantation and the date of first kidney transplantation failure. For those censored kidney transplant recipients, the measure for follow up days was calculated as days between their first transplantation dates and their censored dates. Since the average skipped HD sessions in a month are mostly zeros, and then >0, I use a binary measure for non-adherence, coded "1" if average skipped HD sessions is greater than 0, and "0" if average skipped HD sessions is 0, to estimate this association to check for non-linear effects.

Patient characteristics

Age in six categories (<18, 18-44, 45-59, 60-69, 70-79, and >80), sex, race, body surface area (Dubois formula: $BSA(m^2) = 0.20247 \times Height(m)^{0.725} \times Weight(kg)^{0.425}$), a low BMI indicator (BMI<18.5 kg/m^2), duration of renal replacement therapy, and 37 functional statuses and comorbidities were included to control for exogenous factors that may also have an influence on kidney transplantation failure.

Data for the measures of patient characteristics were obtained from the ESRD Medical Evidence Report (CMS Form 2728) and/or Medicare claims. Clinical comorbidities were obtained from both CMS Form 2728 and/or Medicare claims, since evidence shows that there were issues concerning underreporting of comorbidities using only CMS Form 2728. Additionally, this Medical Evidence Report does not capture changes in patients' comorbidities after the initiation of RRT. Comorbid conditions based purely on this form were not perfectly measured. Thus, clinical comorbidity conditions were based on diagnosis codes reported on Medicare inpatient, outpatient, skilled nursing facility, home health, hospice, and physician claims covering a specified period of time.

These claims-based comorbidity measures were limited to recent diagnoses (i.e., during the previous six months only) for acute conditions such as gastrointestinal bleeding. Longer periods were used for chronic conditions. Several "look back" periods (i.e., diagnoses in last year vs. last two years) were tested to determine their ability to predict costs. The most predictive look back period was chosen as the measure of the comorbidity to be entered into the regression models.

Results

Descriptive analysis

For these 18,393 kidney transplant recipients, 17 percent experienced a kidney transplantation failure, with an average duration from kidney transplantation to kidney transplantation failure of 262 days (Table 4-1). The average number of HD sessions skipped in a month is 0.036 (SD=0.12). 23 percent of the transplant recipients had a record of skipping HD sessions. For the 397,770 HD patients who did not have kidney transplantation, the average HD sessions skipped in a month is 0.061 (SD=0.16). 29 percent of these HD patients had a record of skipped HD sessions. Compared to HD patients without kidney transplantation, kidney transplant recipients are younger, more likely to be male, and slightly more likely to be Asians. They have larger body surface area and are less likely to be underweight. These kidney transplant recipients have a higher ratio of being on dialysis treatments for three years or more. They have lower mean percentages on 28 out of the 37 functional statuses and comorbidities compared to non-recipients. The differences in average HD sessions skipped, demographic variables, patient characteristics, and comorbidities between kidney transplant recipients and non-recipients are mostly statistically significant at the $p < 0.0001$ level.

Regression analysis

Table 4-2 through Table 4-7 list the results for the six Cox proportional hazards models which adjusted for a different set of covariates. Model 1 (Table 4-2), the unadjusted model, shows that if a kidney transplant recipient had, on average, one skipped HD sessions in a month pre-transplant, there would be an 18 percentage increase in kidney transplantation failure. However, this estimate is not statistically significant. Model 2 (Table 4-3) adjusts for patient demographics, duration of renal replacement therapy, body surface area, and low BMI. The hazard ratio dropped from 1.18 to 1.05, which is statistically insignificant. Model 3 (Table 4-4) adjusts for 37 additional functional status and comorbidities. The regression results show that the hazard ratio increased slightly from 1.05 to 1.08, and remained statistically insignificant. Interestingly, the hazard ratios on non-adherence fluctuate somewhat and are statistically insignificant, despite the fact that each model uses a different set of covariates. This suggests that the finding of no association between non-adherence and kidney transplantation failure is a strong and consistent result. This finding supports the "specific non-adherence" conceptual model.

To check for whether there is a non-linear effect, models 4 through 6 resembled models 1 through 3, the only difference being the non-adherence measure. I used a binary variable to replace the linear variable, and re-examined the relationship between non-adherence and kidney transplantation failure. Model 4 shows that if a kidney transplant recipient had a history of skipping HD sessions pre-transplant, then the hazards of experiencing transplantation failure would be increased by 11 percent, and this association is statistically significant. Model 5 shows that, after partial adjustment for patient characteristics, the hazard ratio dropped from 1.11 to 1.07, and became statistically insignificant. This finding suggests that there are some correlations between

non-adherence and patient characteristics, such that the impact of non-adherence on kidney transplantation failure diminished. Finally, model 6 adjusts for a full list of patient characteristics, and the results are similar to model 5 in that they are statistically insignificant and with a hazard ratio of 1.06.

Sensitivity analysis

We excluded those months with any kind of "event" (e.g., hospitalization, withdrawal, and transfer between facilities) being identified and re-fit all six models. The rationale to exclude these months is based on the fact that they have a zero probability of being identified as missing, according to the way I defined the non-adherence measure. Although in reality, a patient could plausibly have an "event" and also skipped an HD session in a particular month. In order to carefully examine the true effect of missing sessions on kidney transplantation failure, it is important to see how sensitive the hazard ratios are when excluding these "event" months.

Models 7-9 show the results using a linear non-adherence measure (Tables 8-10), and Models 10-12 show the results using a binary non-adherence measure (Tables 11-13). Compared with the results presented in models 1-3, the hazard ratios on non-adherence in models 7-9 are slightly higher and remain statistically insignificant. Remarkably, the hazard ratios on the binary non-adherence measure are statistically significant at the 95 percent confidence interval across models 10-12. Model 10 shows that if a kidney transplant recipient had a history of skipping HD sessions pre-transplant, then the hazards of experiencing transplantation failure would be increased by 13 percent.

Models 11-12 show that, after partial and full adjustment for patient characteristics, the hazard ratios dropped from 1.13 to 1.10. This finding suggests that compared with transplant patients who never skipped any HD treatments, transplant patients with a history of missing HD treatments would have a 10 percent increase in hazards of experiencing kidney transplantation failure.

Discussion

One of the primary concerns for transplantation centers is to have a successful recipient of an organ transplant lose the graft due to non-adherence (Garcia et al., 1997). Transplant is the best treatment for ESRD patients. Due to the short supply of transplantable organs, the allocation of organs to ESRD patients on the waitlist who will yield the best transplantation results is an important research and policy issue. In a previous study (Schweizer et al., 1990), 91% of the loss of allograft function or death in kidney transplant recipients was due to non-adherence. Informed decisions should be made to minimize losing organs secondary to non-adherence.

The findings of this study seem to support the fact that adherent patients are more favored in being selected to receive kidney transplantations. It would be in the patient's interest to be adherent in receiving routine HD treatments in order to increase the likelihood of receiving kidney transplantation.

In contrast to previous studies using medication regimens as the non-adherence measure, this study found that there is no association between non-adherence in HD sessions and kidney transplantation failure. From a policy perspective, this finding is

encouraging in two aspects. Increasing medical costs arising from a failed organ are not associated with pre-transplant non-adherence. When evaluating the KAS system, non-adherence in HD sessions may not need to be included in calculating the allocation score, and should not affect a patient's status on the waitlist. Since there is no association between non-adherence in HD sessions pre-transplant, and non-adherence in taking immunosuppressant drugs post-transplant, it may not be cost-effective to allocate medical resources to provide pre-transplant counseling interventions on these targeted non-adherent HD patients. From a dialysis patient's perspective, it would be advantageous to adhere to HD treatments to potentially increase the likelihood of receiving a kidney transplantation, though adherence would not decrease the likelihood of kidney transplantation failure. It is noteworthy to address that in a sensitivity analysis in which months with any kind of events were excluded, I did observe an association between a binary non-adherence measure and kidney transplantation failure. Thus, whether the CMS should allocate medical resources to improve the adherence rate of these HD patients with a history of skipping sessions in order to lower the possibility of kidney transplantation failure requires more refined research.

There are a few limitations of this study. First, the empirical analysis presented only looks at transplantation data from 2004-2006. Findings may not be applicable to other time periods. Next, the analysis also did not take into account the impact of non-adherence in HD sessions on multiple transplantation and multiple transplantation failures. Further, the costs on kidney transplantation vary largely based on whether a kidney is received by a living or deceased donor. Since I do not have this information from my available data set, I am not able to address this concern. Lastly, non-adherence,

as defined in this study, is measured conservatively. For instance, if a patient is identified to have an event (e.g., hospitalization) in a month, then he will not be defined as a "skipped" patient for that month based on my identification strategy. In reality, he might be both "hospitalized" and "non-adherent" for that month. For months with 31 days, patients may receive 13 treatments instead of 12 treatments. Suppose a record shows that a patient received 11 treatments in a 31-day month, without any other event being identified. Using my identification strategy, this patient would be reported as skipping one treatment, although in reality he skipped two treatments. To the extent that this non-adherence measure was underestimated, the prevalence of average HD sessions skipped in a month should be greater than 0.036, and the coefficient estimates on non-adherence as well as other covariates could also be affected. Future research could be conducted to further explore this interesting research topic.

Table 4-1 Summary statistics of all variables, 2004-2006

	Kidney transplant recipients		HD Patients without transplantation		
Variables	Mean	S.D.	Mean	S.D.	Two sample t-test
Dependent variables					
Kidney transplantation failure: binary variable	0.17	0.38	-	-	-
Independent variable of interest					
Average HD sessions skipped in a month	0.036	0.12	0.061	0.16	p <.0001
Average skipped sessions in a month > 0 (Binary variable)	0.23	0.42	0.29	0.45	p <.0001
Follow up days from kidney transplantation to transplantation failure	261.85	926.39	-	-	-
Demographic variables					
Ages <18 yrs	0.012	0.11	0.001	0.03	p <.0001
Ages 18-44 yrs	0.35	0.47	0.11	0.31	p <.0001
Ages 45-59 yrs	0.38	0.47	0.23	0.41	p <.0001
Ages 60-69 yrs	0.21	0.40	0.23	0.41	p <.0001
Ages 70-79 yrs	0.056	0.22	0.27	0.43	p <.0001
Ages 80+ yrs	0.002	0.04	0.16	0.36	p <.0001
Female	0.37	0.48	0.47	0.50	p <.0001
Race: Native American	0.014	0.12	0.014	0.12	p=0.868
Race: Asian	0.051	0.22	0.032	0.18	p <.0001
Race: Black	0.34	0.47	0.35	0.48	p <.0001
Race: White	0.58	0.49	0.59	0.49	p=0003
Race: Other	0.019	0.13	0.010	0.10	p <.0001
Race: Unknown/missing	0.0005	0.02	0.0003	0.02	p=0.186
Patient characteristics and Comorbidities					
Body surface area (Dubois formula)	1.89	0.25	1.86	0.24	p <.0001
Underweight (BMI <18.5 kg/m^2)	0.039	0.18	0.05	0.18	p <.0001
Started RRT during month	0.006	0.05	0.037	0.14	p <.0001
1 previous month of RRT	0.010	0.06	0.062	0.17	p <.0001
2 previous months of RRT	0.008	0.05	0.042	0.11	p <.0001
3 previous months of RRT	0.018	0.07	0.043	0.11	p <.0001
4 previous months of RRT	0.016	0.05	0.034	0.08	p <.0001
5 previous months of RRT	0.016	0.05	0.029	0.07	p <.0001
6 previous months of RRT	0.015	0.05	0.025	0.06	p <.0001
7 previous months of RRT	0.014	0.05	0.024	0.06	p <.0001
8 previous months of RRT	0.013	0.04	0.021	0.05	p <.0001
9 previous months of RRT	0.013	0.04	0.019	0.05	p <.0001
10-12 previous months of RRT	0.040	0.11	0.051	0.10	p <.0001
2nd year of RRT	0.13	0.25	0.14	0.23	p <.0001
3rd year of RRT	0.15	0.28	0.11	0.21	p <.0001
3 years or more of RRT	0.55	0.46	0.36	0.45	p <.0001
Inability to ambulate (2728)	0.005	0.07	0.041	0.20	p <.0001

Inability to transfer (2728)	0.001	0.03	0.016	0.13	p <.0001
Smoking	0.019	0.12	0.035	0.17	p <.0001
Alcohol Dependence between 1999-2004	0.033	0.17	0.055	0.22	p <.0001
Drug Dependence between 1999-2004	0.025	0.15	0.041	0.19	p <.0001
Cardiac Arrest within one year	0.005	0.06	0.017	0.11	p <.0001
Cardiac dysrhythmia within one year	0.20	0.34	0.39	0.42	p <.0001
Ischemic heart disease within one year	0.35	0.42	0.55	0.44	p <.0001
Pericarditis within one year	0.013	0.09	0.012	0.09	p=0.268
Cerebrovascular disease within one year	0.14	0.29	0.30	0.39	p <.0001
Diabetes within one year	0.42	0.46	0.62	0.45	p <.0001
Peripheral vascular disease within one year	0.30	0.39	0.48	0.42	p <.0001
Chronic obstructive pulmonary disease within one year	0.15	0.31	0.33	0.41	p <.0001
Acquired immunodeficiency disease within one year	0.006	0.07	0.015	0.12	p <.0001
Human immnodeficiency virus within one year	0.004	0.06	0.011	0.10	p <.0001
Bacterial Pneumonia six months ago	0.002	0.02	0.006	0.04	p <.0001
Hepatitis B within one year	0.015	0.10	0.012	0.09	p=0.002
Other Hepatitis between 1999-2004	0.076	0.26	0.063	0.24	p <.0001
Opportunistic Infection six months ago	0.002	0.02	0.002	0.02	p=0.584
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.002	0.02	0.003	0.025	p <.0001
Septicemia within six months	0.024	0.08	0.037	0.103	p <.0001
Gastro-Intestinal (GI) Tract Bleeding six months ago	0.002	0.02	0.004	0.032	p <.0001
GI Ulcer - no hemorrhage within six months	0.004	0.03	0.007	0.042	p <.0001
Esophogeal Varices within six months	0.001	0.02	0.0006	0.013	p=0.852
Acquired Hemolytic Anemias within one year	0.018	0.12	0.015	0.109	p=0.0002
Hereditary Hemolytic Anemias between 1999-2004	0.015	0.12	0.018	0.129	p <.0001
Sickle-Cell Anemia between 1999-2004	0.004	0.06	0.004	0.063	p=0.539
Leukemia within one year	0.003	0.05	0.007	0.07	p <.0001
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.004	0.05	0.018	0.12	p <.0001
Lymphoma within two years	0.005	0.07	0.009	0.09	p <.0001
Metastatic Cancers within one year	0.004	0.05	0.021	0.13	p <.0001
Multiple Myeloma within one year	0.002	0.04	0.015	0.12	p <.0001
Breast, Prostate, Colorectal and Other Cancers within one year	0.043	0.18	0.094	0.27	p <.0001
Hyperparathyroidism within one year	0.12	0.29	0.094	0.25	p <.0001
Monoclonal Gammopathy within one year	0.003	0.05	0.009	0.09	p <.0001
Myelofibrosis within one year	0.005	0.06	0.005	0.06	p=0.461
Myelodysplastic Syndrome between 1999-2004	0.005	0.07	0.016	0.12	p <.0001
N	18,393		397,770		

Table 4-2 Results from the Cox proportional hazards models, 2004-2006

	Model 1 - Unadjusted			
Variable	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Average skipped HD sessions in a month	1.18	0.88	1.56	0.2676
Observations	18,393			

Table 4-3 Results from the Cox proportional hazards models, 2004-2006 (cont'd)

Variables	Model 2 - Adjusted for patient demographics, time since start of RRT, body surface area, and low BMI			
	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Average skipped HD sessions in a month	1.05	0.78	1.41	0.748
Demographic variables				
Ages <18 yrs	1.00	0.72	1.40	0.995
Ages 18-44 yrs	0.83	0.75	0.93	0.001
Ages 45-59 yrs	0.79	0.71	0.88	<.0001
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.19	0.97	1.47	0.097
Ages 80+ yrs	3.11	1.21	7.97	0.018
Female	1.01	0.93	1.09	0.863
Race: Native American	1.10	0.79	1.54	0.576
Race: Asian	1.32	1.10	1.58	0.003
Race: Black	1.50	1.38	1.62	<.0001
Race: White	ref.	-	-	-
Race: Other	1.38	1.02	1.86	0.038
Race: Unknown/missing	7.82	1.11	55.32	0.039
Patient characteristics and Comorbidities				
Started RRT during month	2.70	0.76	9.59	0.123
1 previous month of RRT	2.34	0.44	12.43	0.319
2 previous months of RRT	2.85	0.66	12.26	0.160
3 previous months of RRT	1.87	0.65	5.38	0.247
4 previous months of RRT	3.46	0.57	21.03	0.178
5 previous months of RRT	2.75	0.43	17.58	0.284
6 previous months of RRT	6.62	1.03	42.67	0.047
7 previous months of RRT	1.44	0.40	5.22	0.581
8 previous months of RRT	3.39	0.83	13.82	0.089
9 previous months of RRT	2.30	0.57	9.28	0.241
10-12 previous months of RRT	2.31	1.39	3.85	0.001
2nd year of RRT	2.80	2.28	3.43	<.0001
3rd year of RRT	3.20	2.71	3.78	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.33	1.10	1.60	0.003
Underweight (BMI <18.5 kg/m^2)	0.96	0.79	1.16	0.678
Observations	18,393			

Table 4-4 Results from the Cox proportional hazards models, 2004-2006 (cont'd)

	Model 3 - Model 2 +37 functional status and comorbidities			
Variables	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Average skipped HD sessions in a month	1.08	0.80	1.46	0.6185
Demographic variables				
Ages <18 yrs	1.14	0.81	1.61	0.4632
Ages 18-44 yrs	0.90	0.80	1.01	0.0738
Ages 45-59 yrs	0.82	0.73	0.92	0.0007
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.17	0.95	1.45	0.1503
Ages 80+ yrs	2.95	1.15	7.54	0.0239
Female	0.99	0.91	1.08	0.8564
Race: Native American	1.03	0.73	1.44	0.8874
Race: Asian	1.35	1.13	1.62	0.001
Race: Black	1.52	1.41	1.65	<.0001
Race: White	ref.	-	-	-
Race: Other	1.39	1.03	1.88	0.0328
Race: Unknown/missing	7.69	1.08	54.51	0.0413
Patient characteristics and Comorbidities				
Started RRT during month	2.72	0.80	9.22	0.1093
1 previous month of RRT	1.31	0.22	7.69	0.768
2 previous months of RRT	3.70	0.90	15.30	0.0703
3 previous months of RRT	2.15	0.76	6.05	0.1476
4 previous months of RRT	2.97	0.46	19.13	0.253
5 previous months of RRT	2.87	0.43	19.32	0.2791
6 previous months of RRT	6.41	0.96	42.86	0.0554
7 previous months of RRT	1.64	0.44	6.06	0.4608
8 previous months of RRT	2.96	0.74	11.90	0.1267
9 previous months of RRT	2.14	0.55	8.23	0.2701
10-12 previous months of RRT	2.24	1.35	3.73	0.0019
2nd year of RRT	2.65	2.16	3.26	<.0001
3rd year of RRT	3.10	2.62	3.68	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.31	1.08	1.58	0.0051
Underweight (BMI <18.5 kg/m^2)	0.95	0.78	1.16	0.617
Inability to ambulate (2728)	0.74	0.41	1.31	0.2966
Inability to transfer (2728)	3.73	1.38	10.08	0.0094
Smoking	1.41	1.03	1.94	0.0328
Alcohol Dependence between 1999-2004	1.14	0.94	1.39	0.1781
Drug Dependence between 1999-2004	1.04	0.85	1.26	0.7214
Cardiac Arrest within one year	1.41	0.85	2.34	0.1798
Cardiac dysrhythmia within one year	1.09	0.98	1.21	0.115
Ischemic heart disease within one year	0.96	0.88	1.06	0.4629
Pericarditis within one year	0.97	0.68	1.37	0.8542
Cerebrovascular disease within one year	1.03	0.91	1.17	0.6159

Diabetes within one year	1.24	1.14	1.35	<.0001
Peripheral vascular disease within one year	1.14	1.03	1.25	0.0079
Chronic obstructive pulmonary disease within one year	1.02	0.91	1.15	0.684
Acquired immunodeficiency disease within one year	1.52	0.89	2.57	0.1234
Human immnodeficiency virus within one year	1.34	0.74	2.43	0.329
Bacterial Pneumonia six months ago	0.68	0.13	3.54	0.645
Hepatitis B within one year	0.90	0.65	1.24	0.5052
Other Hepatitis between 1999-2004	0.93	0.82	1.05	0.2311
Opportunistic Infection six months ago	2.31	0.64	8.33	0.1996
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.39	0.06	2.67	0.334
Septicemia within six months	0.96	0.64	1.45	0.8536
Gastro-Intestinal (GI) Tract Bleeding six months ago	1.26	0.39	4.10	0.6997
GI Ulcer - no hemorrhage within six months	0.97	0.28	3.36	0.9656
Esophogeal Varices within six months	3.49	0.47	25.63	0.2199
Acquired Hemolytic Anemias within one year	1.14	0.88	1.47	0.3159
Hereditary Hemolytic Anemias between 1999-2004	0.94	0.73	1.22	0.6466
Sickle-Cell Anemia between 1999-2004	1.25	0.78	2.02	0.3496
Leukemia within one year	0.78	0.37	1.67	0.5275
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	1.11	0.66	1.88	0.6861
Lymphoma within two years	0.71	0.47	1.07	0.0995
Metastatic Cancers within one year	2.38	1.15	4.93	0.0201
Multiple Myeloma within one year	3.06	1.24	7.53	0.0148
Breast, Prostate, Colorectal and Other Cancers within one year	0.89	0.73	1.07	0.2147
Hyperparathyroidism within one year	1.01	0.90	1.13	0.9108
Monoclonal Gammopathy within one year	0.94	0.47	1.90	0.8683
Myelofibrosis within one year	1.39	0.76	2.52	0.2825
Myelodysplastic Syndrome between 1999-2004	0.90	0.61	1.32	0.5747
Observations			18,393	

Table 4-5 Results from the Cox proportional hazards models, sensitivity analysis (binary skipped sessions variable), 2004-2006

	Model 4 - Unadjusted			
Variable	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Binary variable: Average skipped HD sessions in a month > 0	1.11	1.02	1.20	0.0156
Observations		18,393		

Table 4-6 Results from the Cox proportional hazards models, sensitivity analysis (binary skipped sessions variable), 2004-2006 (cont'd)

Variables	Model 5 - Adjusted for patient demographics, time since start of RRT, body surface area, and low BMI			
	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Binary variable: Average skipped HD sessions in a month > 0	1.07	0.98	1.16	0.1134
Demographic variables				
Ages <18 yrs	1.00	0.72	1.40	0.9871
Ages 18-44 yrs	0.83	0.75	0.93	0.0008
Ages 45-59 yrs	0.79	0.71	0.88	<.0001
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.19	0.97	1.47	0.0974
Ages 80+ yrs	3.11	1.22	7.98	0.0179
Female	1.01	0.93	1.09	0.8612
Race: Native American	1.10	0.79	1.54	0.5741
Race: Asian	1.32	1.10	1.58	0.0026
Race: Black	1.49	1.38	1.61	<.0001
Race: White	ref.	-	-	-
Race: Other	1.37	1.02	1.85	0.0382
Race: Unknown/missing	7.90	1.12	55.91	0.0384
Patient characteristics and Comorbidities				
Started RRT during month	2.74	0.77	9.72	0.1179
1 previous month of RRT	2.37	0.45	12.57	0.3124
2 previous months of RRT	2.89	0.67	12.43	0.1532
3 previous months of RRT	1.89	0.66	5.45	0.2371
4 previous months of RRT	3.38	0.55	20.70	0.1885
5 previous months of RRT	2.75	0.43	17.63	0.2871
6 previous months of RRT	6.67	1.03	43.10	0.0462
7 previous months of RRT	1.47	0.41	5.34	0.5561
8 previous months of RRT	3.32	0.81	13.54	0.0948
9 previous months of RRT	2.29	0.56	9.29	0.2479
10-12 previous months of RRT	2.29	1.37	3.83	0.0015
2nd year of RRT	2.79	2.27	3.41	<.0001
3rd year of RRT	3.22	2.72	3.80	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.33	1.11	1.61	0.0025
Underweight (BMI <18.5 kg/m^2)	0.96	0.79	1.16	0.6805
Observations		18,393		

Table 4-7 Results from the Cox proportional hazards models, sensitivity analysis (binary skipped sessions variable), 2004-2006 (cont'd)

	Model 6 - Model 5 +37 functional status and comorbidities			
Variables	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Binary variable: Average skipped HD sessions in a month > 0	1.06	0.98	1.16	0.1649
Demographic variables				
Ages <18 yrs	1.14	0.81	1.61	0.4645
Ages 18-44 yrs	0.90	0.80	1.01	0.0743
Ages 45-59 yrs	0.82	0.73	0.92	0.0007
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.17	0.95	1.45	0.1512
Ages 80+ yrs	2.95	1.16	7.55	0.0237
Female	0.99	0.91	1.08	0.8587
Race: Native American	1.03	0.73	1.44	0.8877
Race: Asian	1.36	1.13	1.62	0.001
Race: Black	1.52	1.40	1.65	<.0001
Race: White	ref.	-	-	-
Race: Other	1.39	1.03	1.88	0.0329
Race: Unknown/missing	7.74	1.09	54.89	0.0406
Patient characteristics and Comorbidities				
Started RRT during month	2.75	0.81	9.32	0.1051
1 previous month of RRT	1.33	0.23	7.82	0.753
2 previous months of RRT	3.74	0.91	15.44	0.0679
3 previous months of RRT	2.17	0.77	6.12	0.1414
4 previous months of RRT	2.92	0.45	18.92	0.2617
5 previous months of RRT	2.87	0.42	19.44	0.2796
6 previous months of RRT	6.44	0.96	43.25	0.0552
7 previous months of RRT	1.66	0.45	6.15	0.4483
8 previous months of RRT	2.91	0.73	11.71	0.1318
9 previous months of RRT	2.13	0.55	8.25	0.2739
10-12 previous months of RRT	2.23	1.34	3.72	0.0021
2nd year of RRT	2.64	2.15	3.25	<.0001
3rd year of RRT	3.12	2.63	3.70	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.31	1.09	1.58	0.0045
Underweight (BMI <18.5 kg/m^2)	0.95	0.78	1.16	0.6201
Inability to ambulate (2728)	0.75	0.42	1.33	0.3167
Inability to transfer (2728)	3.73	1.38	10.08	0.0094
Smoking	1.41	1.03	1.94	0.0342
Alcohol Dependence between 1999-2004	1.14	0.94	1.39	0.1823
Drug Dependence between 1999-2004	1.03	0.85	1.26	0.7402
Cardiac Arrest within one year	1.42	0.85	2.35	0.1778
Cardiac dysrhythmia within one year	1.08	0.98	1.20	0.1298
Ischemic heart disease within one year	0.97	0.88	1.06	0.4768

Pericarditis within one year	0.96	0.68	1.36	0.8288
Cerebrovascular disease within one year	1.04	0.91	1.18	0.6002
Diabetes within one year	1.24	1.14	1.35	<.0001
Peripheral vascular disease within one year	1.13	1.03	1.25	0.0091
Chronic obstructive pulmonary disease within one year	1.02	0.91	1.15	0.7047
Acquired immunodeficiency disease within one year	1.49	0.88	2.54	0.1369
Human immnodeficiency virus within one year	1.35	0.75	2.44	0.3219
Bacterial Pneumonia six months ago	0.68	0.13	3.54	0.6429
Hepatitis B within one year	0.89	0.64	1.24	0.4974
Other Hepatitis between 1999-2004	0.93	0.82	1.05	0.2354
Opportunistic Infection six months ago	2.34	0.65	8.42	0.1921
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.38	0.06	2.66	0.3315
Septicemia within six months	0.96	0.64	1.45	0.844
Gastro-Intestinal (GI) Tract Bleeding six months ago	1.30	0.40	4.22	0.6676
GI Ulcer - no hemorrhage within six months	0.99	0.29	3.42	0.9882
Esophogeal Varices within six months	3.47	0.47	25.54	0.222
Acquired Hemolytic Anemias within one year	1.14	0.88	1.47	0.3177
Hereditary Hemolytic Anemias between 1999-2004	0.94	0.73	1.22	0.6604
Sickle-Cell Anemia between 1999-2004	1.26	0.78	2.02	0.3481
Leukemia within one year	0.80	0.37	1.69	0.5511
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	1.12	0.66	1.88	0.6776
Lymphoma within two years	0.71	0.47	1.07	0.1
Metastatic Cancers within one year	2.35	1.13	4.89	0.0217
Multiple Myeloma within one year	3.04	1.23	7.51	0.0158
Breast, Prostate, Colorectal and Other Cancers within one year	0.88	0.73	1.07	0.1962
Hyperparathyroidism within one year	1.01	0.90	1.13	0.8479
Monoclonal Gammopathy within one year	0.93	0.46	1.87	0.8439
Myelofibrosis within one year	1.40	0.77	2.54	0.2724
Myelodysplastic Syndrome between 1999-2004	0.89	0.61	1.32	0.5666
Observations			18,393	

Table 4-8 Results from the Cox proportional hazards models, sensitivity analysis (the exclusion of any kind of event), 2004-2006

	Model 7 - Unadjusted			
Variable	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Average skipped HD sessions in a month	1.20	0.93	1.54	0.1619
Observations		18,393		

Table 4-9 Results from the Cox proportional hazards models, sensitivity analysis (the exclusion of any kind of event), 2004-2006 (cont'd)

	Model 8 - Adjusted for patient demographics, time since start of RRT, body surface area, and low BMI			
Variables	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Average skipped HD sessions in a month	1.07	0.83	1.39	0.5983
Demographic variables				
Ages <18 yrs	1.09	0.79	1.50	0.5948
Ages 18-44 yrs	0.85	0.76	0.95	0.0025
Ages 45-59 yrs	0.81	0.73	0.91	0.0002
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.18	0.96	1.44	0.1111
Ages 80+ yrs	2.57	0.89	7.39	0.0806
Female	1.01	0.93	1.09	0.844
Race: Native American	1.11	0.79	1.56	0.5571
Race: Asian	1.35	1.12	1.61	0.0012
Race: Black	1.49	1.38	1.61	<.0001
Race: White	ref.	-	-	-
Race: Other	1.43	1.07	1.93	0.0172
Race: Unknown/missing	12.88	1.82	91.35	0.0106
Patient characteristics and Comorbidities				
Started RRT during month	4.09	1.32	12.64	0.0145
1 previous month of RRT	3.75	0.94	14.90	0.0604
2 previous months of RRT	3.94	1.29	12.00	0.0158
3 previous months of RRT	2.86	1.39	5.88	0.0045
4 previous months of RRT	2.75	0.58	13.09	0.2047
5 previous months of RRT	4.86	1.08	21.83	0.0393
6 previous months of RRT	4.12	0.82	20.80	0.0863
7 previous months of RRT	2.17	0.86	5.50	0.1022
8 previous months of RRT	3.03	1.04	8.87	0.0426
9 previous months of RRT	2.52	0.85	7.45	0.0955
10-12 previous months of RRT	2.91	1.84	4.61	<.0001
2nd year of RRT	3.08	2.55	3.73	<.0001
3rd year of RRT	3.55	3.03	4.15	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.43	1.19	1.72	0.0001
Underweight (BMI <18.5 kg/m^2)	0.98	0.81	1.18	0.8098
Observations		18,393		

Table 4-10 Results from the Cox proportional hazards models, sensitivity analysis (the exclusion of any kind of event), 2004-2006 (cont'd)

	Model 9 - Model 8 +37 functional statuses and comorbidities			
Variables	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Average skipped HD sessions in a month	1.08	0.83	1.41	0.560
Demographic variables				
Ages <18 yrs	1.20	0.86	1.67	0.276
Ages 18-44 yrs	0.90	0.80	1.01	0.073
Ages 45-59 yrs	0.83	0.74	0.93	0.002
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.15	0.94	1.41	0.186
Ages 80+ yrs	2.40	0.84	6.91	0.104
Female	1.00	0.92	1.08	0.950
Race: Native American	1.02	0.73	1.44	0.900
Race: Asian	1.36	1.14	1.63	0.001
Race: Black	1.51	1.40	1.64	<.0001
Race: White	ref.	-	-	-
Race: Other	1.43	1.06	1.93	0.018
Race: Unknown/missing	12.77	1.80	90.75	0.011
Patient characteristics and Comorbidities				
Started RRT during month	3.71	1.20	11.50	0.023
1 previous month of RRT	3.94	0.99	15.70	0.052
2 previous months of RRT	3.59	1.09	11.81	0.035
3 previous months of RRT	3.13	1.53	6.43	0.002
4 previous months of RRT	2.48	0.51	12.11	0.262
5 previous months of RRT	5.20	1.17	23.18	0.031
6 previous months of RRT	4.13	0.84	20.32	0.081
7 previous months of RRT	2.32	0.91	5.92	0.079
8 previous months of RRT	2.59	0.90	7.49	0.079
9 previous months of RRT	2.41	0.83	7.01	0.108
10-12 previous months of RRT	2.77	1.74	4.40	<.0001
2nd year of RRT	2.97	2.45	3.60	<.0001
3rd year of RRT	3.44	2.93	4.04	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.40	1.17	1.68	0.000
Underweight (BMI <18.5 kg/m^2)	0.99	0.82	1.20	0.903
Inability to ambulate (2728)	0.76	0.43	1.35	0.353
Inability to transfer (2728)	2.62	0.91	7.54	0.074
Smoking	1.43	1.04	1.96	0.029
Alcohol Dependence between 1999-2004	1.14	0.94	1.38	0.192
Drug Dependence between 1999-2004	1.02	0.84	1.23	0.885
Cardiac Arrest within one year	1.17	0.71	1.92	0.541
Cardiac dysrhythmia within one year	1.05	0.95	1.17	0.308
Ischemic heart disease within one year	0.97	0.88	1.06	0.503

Pericarditis within one year	0.89	0.64	1.23	0.477
Cerebrovascular disease within one year	1.03	0.91	1.16	0.680
Diabetes within one year	1.22	1.13	1.33	<.0001
Peripheral vascular disease within one year	1.13	1.03	1.23	0.011
Chronic obstructive pulmonary disease within one year	1.01	0.91	1.13	0.816
Acquired immunodeficiency disease within one year	1.57	0.95	2.60	0.080
Human immnodeficiency virus within one year	1.33	0.75	2.36	0.337
Bacterial Pneumonia six months ago	1.22	0.36	4.20	0.748
Hepatitis B within one year	0.89	0.65	1.23	0.489
Other Hepatitis between 1999-2004	0.93	0.82	1.04	0.204
Opportunistic Infection six months ago	0.99	0.28	3.58	0.992
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.59	0.09	3.99	0.590
Septicemia within six months	0.90	0.62	1.29	0.559
Gastro-Intestinal (GI) Tract Bleeding six months ago	1.80	0.68	4.74	0.235
GI Ulcer - no hemorrhage within six months	0.92	0.33	2.56	0.867
Esophogeal Varices within six months	2.59	0.52	13.02	0.247
Acquired Hemolytic Anemias within one year	1.08	0.84	1.39	0.555
Hereditary Hemolytic Anemias between 1999-2004	0.91	0.71	1.16	0.431
Sickle-Cell Anemia between 1999-2004	1.14	0.69	1.87	0.612
Leukemia within one year	0.80	0.37	1.73	0.572
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.96	0.55	1.67	0.887
Lymphoma within two years	0.71	0.47	1.06	0.090
Metastatic Cancers within one year	2.39	1.00	5.71	0.049
Multiple Myeloma within one year	2.14	0.76	5.99	0.148
Breast, Prostate, Colorectal and Other Cancers within one year	0.80	0.67	0.97	0.022
Hyperparathyroidism within one year	1.01	0.90	1.12	0.907
Monoclonal Gammopathy within one year	1.18	0.60	2.34	0.636
Myelofibrosis within one year	1.22	0.73	2.04	0.445
Myelodysplastic Syndrome between 1999-2004	0.86	0.58	1.26	0.441
Observations			18,393	

Table 4-11 Results from the Cox proportional hazards models, sensitivity analysis (binary skipped sessions variable and the exclusion of any kind of event), 2004-2006

	Model 10 - Unadjusted			
Variable	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Binary variable: Average skipped HD sessions in a month > 0	1.13	1.04	1.23	0.003
Observations		18,393		

Table 4-12 Results from the Cox proportional hazards models, sensitivity analysis (binary skipped sessions variable and the exclusion of any kind of event), 2004-2006 (cont'd)

Variables	Model 11 - Adjusted for patient demographics, time since start of RRT, body surface area, and low BMI			
	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Binary variable: Average skipped HD sessions in a month > 0	1.10	1.01	1.20	0.0228
Demographic variables				
Ages <18 yrs	1.09	0.79	1.50	0.5972
Ages 18-44 yrs	0.85	0.76	0.94	0.0024
Ages 45-59 yrs	0.81	0.73	0.91	0.0002
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.18	0.97	1.45	0.1016
Ages 80+ yrs	2.57	0.89	7.40	0.0803
Female	1.01	0.93	1.09	0.8604
Race: Native American	1.11	0.79	1.55	0.5601
Race: Asian	1.35	1.13	1.61	0.0012
Race: Black	1.48	1.38	1.60	<.0001
Race: White	ref.	-	-	-
Race: Other	1.43	1.07	1.93	0.0176
Race: Unknown/missing	13.05	1.84	92.58	0.0102
Patient characteristics and Comorbidities				
Started RRT during month	4.17	1.35	12.87	0.0132
1 previous month of RRT	3.76	0.94	15.01	0.0603
2 previous months of RRT	4.02	1.32	12.24	0.0143
3 previous months of RRT	2.89	1.40	5.95	0.0041
4 previous months of RRT	2.69	0.56	12.91	0.2159
5 previous months of RRT	4.94	1.10	22.25	0.0376
6 previous months of RRT	3.97	0.78	20.13	0.0959
7 previous months of RRT	2.23	0.88	5.64	0.0911
8 previous months of RRT	3.06	1.05	8.97	0.0412
9 previous months of RRT	2.47	0.83	7.37	0.1063
10-12 previous months of RRT	2.91	1.83	4.61	<.0001
2nd year of RRT	3.06	2.53	3.70	<.0001
3rd year of RRT	3.57	3.05	4.18	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.44	1.20	1.73	<.0001
Underweight (BMI <18.5 kg/m^2)	0.98	0.81	1.18	0.8123
Observations	18,393			

Table 4-13 Results from the Cox proportional hazards models, sensitivity analysis (binary skipped sessions variable and the exclusion of any kind of event), 2004-2006 (cont'd)

	Model 12 - Model 11 +37 functional statuses and comorbidities			
Variables	H.R.	95% CI		Pr > Chi
Independent variable of interest				
Binary variable: Average skipped HD sessions in a month > 0	1.10	1.01	1.19	0.0338
Demographic variables				
Ages <18 yrs	1.20	0.86	1.67	0.2824
Ages 18-44 yrs	0.90	0.80	1.01	0.0719
Ages 45-59 yrs	0.83	0.74	0.93	0.0017
Ages 60-69 yrs	ref.	-	-	-
Ages 70-79 yrs	1.15	0.94	1.41	0.1737
Ages 80+ yrs	2.41	0.84	6.93	0.1028
Female	1.00	0.92	1.08	0.9366
Race: Native American	1.02	0.73	1.44	0.9038
Race: Asian	1.36	1.14	1.63	0.0008
Race: Black	1.51	1.39	1.63	<.0001
Race: White	ref.	-	-	-
Race: Other	1.44	1.07	1.93	0.0176
Race: Unknown/missing	12.91	1.82	91.73	0.0106
Patient characteristics and Comorbidities				
Started RRT during month	3.78	1.22	11.71	0.0212
1 previous month of RRT	3.92	0.98	15.66	0.0534
2 previous months of RRT	3.69	1.12	12.09	0.0313
3 previous months of RRT	3.16	1.54	6.49	0.0017
4 previous months of RRT	2.44	0.50	12.00	0.2715
5 previous months of RRT	5.27	1.18	23.57	0.0296
6 previous months of RRT	4.00	0.81	19.80	0.0893
7 previous months of RRT	2.37	0.93	6.04	0.0716
8 previous months of RRT	2.62	0.91	7.57	0.0756
9 previous months of RRT	2.36	0.80	6.96	0.118
10-12 previous months of RRT	2.77	1.74	4.40	<.0001
2nd year of RRT	2.95	2.44	3.58	<.0001
3rd year of RRT	3.46	2.94	4.06	<.0001
3 years or more of RRT	ref.	-	-	-
Body surface area (Dubois formula)	1.41	1.17	1.69	0.0002
Underweight (BMI <18.5 kg/m^2)	0.99	0.82	1.20	0.903
Inability to ambulate (2728)	0.78	0.44	1.37	0.3835
Inability to transfer (2728)	2.62	0.91	7.55	0.0735
Smoking	1.42	1.03	1.95	0.0319
Alcohol Dependence between 1999-2004	1.14	0.94	1.38	0.1968
Drug Dependence between 1999-2004	1.01	0.83	1.23	0.9226
Cardiac Arrest within one year	1.17	0.71	1.93	0.5282
Cardiac dysrhythmia within one year	1.05	0.95	1.16	0.3396
Ischemic heart disease within one year	0.97	0.88	1.07	0.5331

Pericarditis within one year	0.88	0.63	1.22	0.4453
Cerebrovascular disease within one year	1.03	0.91	1.16	0.6435
Diabetes within one year	1.23	1.13	1.33	<.0001
Peripheral vascular disease within one year	1.12	1.03	1.23	0.0128
Chronic obstructive pulmonary disease within one year	1.01	0.91	1.13	0.8382
Acquired immunodeficiency disease within one year	1.53	0.92	2.54	0.0981
Human immnodeficiency virus within one year	1.34	0.75	2.38	0.3253
Bacterial Pneumonia six months ago	1.21	0.35	4.17	0.7613
Hepatitis B within one year	0.89	0.65	1.23	0.4853
Other Hepatitis between 1999-2004	0.93	0.83	1.04	0.2173
Opportunistic Infection six months ago	1.01	0.28	3.64	0.9895
Pneumococcal pneumonia, emphysema, lung abcess within six months	0.61	0.09	4.13	0.6116
Septicemia within six months	0.89	0.62	1.28	0.5233
Gastro-Intestinal (GI) Tract Bleeding six months ago	1.86	0.70	4.90	0.2107
GI Ulcer - no hemorrhage within six months	0.93	0.33	2.60	0.8889
Esophogeal Varices within six months	2.60	0.52	13.06	0.2458
Acquired Hemolytic Anemias within one year	1.08	0.84	1.38	0.5633
Hereditary Hemolytic Anemias between 1999-2004	0.91	0.71	1.16	0.4565
Sickle-Cell Anemia between 1999-2004	1.14	0.69	1.87	0.6081
Leukemia within one year	0.82	0.38	1.77	0.6062
Lung, Upper Digestive Tract, and Other Severe Cancers within one year	0.96	0.56	1.67	0.8887
Lymphoma within two years	0.71	0.47	1.06	0.0911
Metastatic Cancers within one year	2.41	1.01	5.76	0.0477
Multiple Myeloma within one year	2.11	0.75	5.95	0.1591
Breast, Prostate, Colorectal and Other Cancers within one year	0.80	0.66	0.96	0.0189
Hyperparathyroidism within one year	1.01	0.91	1.13	0.8247
Monoclonal Gammopathy within one year	1.15	0.58	2.29	0.6811
Myelofibrosis within one year	1.23	0.74	2.05	0.4297
Myelodysplastic Syndrome between 1999-2004	0.85	0.58	1.25	0.419
Observations			18,393	

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Chapter V

Chapter V. Conclusion

Summary of Findings

This dissertation provides important information for policy makers, researchers, dialysis providers, and dialysis patients with respect to how non-adherence would have an effect on health care costs and kidney transplantation failure. Since the CMS implemented a full bundling system on January 1, 2011, the findings from Chapter II are especially salient in understanding how this new bundling system will change implications of skipped treatments for dialysis providers and the CMS. Based on study results which show that skipping sessions is associated with lower SB utilization, with some evidence of slightly more SB utilization in the following months to make up for the missed treatments, it is expected that dialysis providers would find means to reduce non-adherence in order to maximize profit. Facilities can design appointment follow-up programs to target those patients who commonly skip HD treatments. From the CMS perspective, since the bundled payment is made per patient per treatment, there is enough financial incentive for facilities to improve patient adherence because they will not receive reimbursement from a missed session. The CMS probably needs not design

policy intervention in improving patient adherence at this point. Results from this study also show that compared with 2SLS and log-linear estimations, the OLS estimation is a more reliable approach in examining the association of non-adherence on SB MAP. Distance is not a strong and valid instrument in the 2SLS estimation, and future work could be conducted to find a better instrument in order to tackle the endogeneity concern.

Chapter III provides information on whether non-adherence in HD sessions is associated with cost-savings for the providers, using CR costs as the health care costs measure. Results show that there are no meaningful cost-savings for dialysis facilities when patients skipped routine HD treatments. With the presence of non-adherence, total revenues for dialysis facilities are expected to drop due to fewer sessions provided. Consequently, there is a financial incentive for dialysis facilities to improve patient adherence. Since there is no meaning effect of non-adherence on CR costs, policy interventions from the CMS to improve the adherence rate in hemodialysis is dubious. In addition, findings from this study show that log-linear models perform better than OLS models. The concern of retransformation issues when using a log-linear model to estimate health care costs and the need to use a smearing estimator (Duan, 1983) to adjust for heteroscedasticity in error terms need to be studied further. Adding facility characteristics to the models increases the explanatory power.

One of the primary concerns for transplantation centers is to have a successful recipient of an organ transplant lose the graft due to non-adherence (Garcia et al., 1997). Transplant is the best treatment for ESRD patients. Due to the short supply of transplantable organs, the allocation of organs to ESRD patients on the waitlist who will yield the best transplantation results is an important research and policy issue. The

findings of Chapter IV seem to support the fact that adherent patients are more favored in being selected to receive kidney transplantations. From a dialysis patient's perspective, it would be advantageous to adhere to HD treatments to potentially increase the likelihood of receiving a kidney transplantation.

In contrast to previous studies using medication regimens as the non-adherence measure, this study found that there is no association between non-adherence in HD sessions and kidney transplantation failure. From a policy perspective, this finding is encouraging in two aspects. Increasing medical costs arising from a failed organ are not associated with pre-transplant non-adherence. When evaluating the KAS system, non-adherence in HD sessions may not need to be included in calculating the allocation score, and should not affect a patient's status on the waitlist. Since there is no association between non-adherence in HD sessions pre-transplant, and non-adherence in taking immunosuppressant drugs post-transplant, it may not be cost-effective to allocate medical resources to provide pre-transplant counseling interventions on these targeted non-adherent HD patients

Study Limitations

There are a number of limitations pertinent to this dissertation. (1) Non-adherence, as defined in this study, is measured conservatively. To the extent that this non-adherence measure was underestimated, the true prevalence of non-adherence should be greater than presented, and the coefficient estimates on non-adherence as well as other covariates could also be affected. Future research that applies a broader non-adherence measure

incorporating shortened HD sessions by 10 or more minutes, an interdialytic weight gain of more than 5.7 percent or dry weight, and a serum phosphate of greater than 7.5 mg/Dl would be extremely interesting. (2) The empirical analyses presented in three chapters only look at data from 2004-2006, so findings may not be applicable to other time periods. Future research using different time periods to examine the association would be helpful. (3) For Chapters II and III, since I only observe the pattern of health care costs for hemodialysis patients, these findings could not be generalized to patients using other modalities. Future studies can be conducted on peritoneal dialysis patients or home hemodialysis patients. (4) Causal inference between non-adherence and CR costs could not be drawn from Chapter III. (5) Another limitation from Chapter III is related to the quality of Medicare cost report data. Researchers have raised concerns about the incompleteness of the cost report data (Bednar, 1992; Magnus et al., 2000; Medicare Payment Advisory Commission, 2004). Though imperfect, there are several strengths with respect to the cost report data. These data are the only available source of ESRD cost data, and are used widely by researchers and the CMS to modify ESRD payment policy. There is a high correlation between the number of dialysis treatments presented on the cost report and the dialysis treatments reported on Medicare claims data. The CMS has continuously refined the minimum file requirements and reminded providers in terms of "Potential Rejection Errors" to correct for implausible values on the number of treatments and dates. (6) For Chapter III, I did not consider the impact of non-adherence in HD sessions on multiple transplantation and multiple transplantation failures. Future research can be conducted to address this concern.

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