The Timing of Arteriovenous Fistula Placement and Medicare Costs During Dialysis Initiation

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Introduction

Although considered a rare disease in 1972 when its treatment was added to the Medicare program, the incidence and prevalence of total kidney failure, called End Stage Renal Disease (ESRD), has grown substantially in the last half-century. There are now over 500,000 patients with ESRD, comprising about 1% of all Medicare patients but accounting for over 6% of total expenditures. There were over 110,000 incident ESRD patients in 2006, projected to grow to over 150,000 by the year 2020, with a total of almost 800,000 ESRD patients by that time (Gilbertson, 2005; USRDS, 2008, Vol 2, Fig 2.1).

Although kidney transplants have become more common, organ shortages as well as the complex disease burden of patients result in the majority of patients having their ESRD treated by clinic-provided hemodialysis (HD). This process, which represents the type of renal replacement therapy for 90% of new ESRD patients, involves pumping a patient's blood through an external dialysis machine to filter and clean the blood before returning it to the body. This process requires a vascular access be placed in the patient to allow the blood to flow from the patient to the dialysis machine and back again. There are two main types of vascular access: a temporary catheter, which is simply a plastic tube inserted through the skin and into a vein, and an internal access, which connects an artery and vein together to produce a strong location from which blood can be drawn. The internal access is called an arteriovenous fistula (AVF) if the vein and artery are joined directly together. If they are joined with a synthetic tube it is called an arteriovenous graft (AVG). Catheters are quick to insert, cost very little and can be used almost immediately. However, they are prone to infections and complications like clotting. AVFs and AVGs, on the other hand, are surgically created, causing them to be more expensive and require time to mature before they can be used. However, since they are completely internal they are much less at risk for infections and complications.

The National Kidney Foundation (NKF) indicates that AVFs should be the first choice "…because [they] generally last longer and have fewer problems such as infections and clotting" (http://www.kidney.org/patients/plu/plu_intro/pluo_9.cfm, accessed December, 2010). If it is not possible due to small veins or weak blood vessels, the second choice should be an AVG, while catheters are really meant to be temporary solutions. A collection of dialysis providers, insurers, and others including the Center for Medicare and Medicaid Services (CMS), the Center for Disease Control (CDC), NKF, and the division of the National Institutes of Health associated with kidney disease (National Institute for Diabetes, Digestive and Kidney Disorders, or NIDDK) have formed a coalition called "Fistula First" with the goal of increasing the use of AVFs in patients for

whom it is appropriate, indicating that “AVFs last longer, need less rework or repairs, and are associated with lower rates of infection, hospitalization and death” (www.fistulafirst.org, main page, left-hand banner, accessed 7/8/2009).

Clinically, then, it is clear that AVFs are preferred, and that ideally patients would have them placed as early as possible. In fact, clinical guidelines recommend placing them *before* the start of dialysis. These guidelines, established by NKF, indicate that patients should have a functioning permanent access (i.e. AVF or AVG) when they begin dialysis, adding that AVFs should be placed “at least 6 months before the anticipated start of HD treatments” and AVGs at least 3 to 6 weeks prior (NKF, 2006). Healthy People 2010 states Objective 4-4 as: “Increase the proportion of new HD patients who use AVFs as their primary mode of vascular access” (US DHHS, 2000). If it can be shown that placing AVFs early also saves overall costs, then the preferred health policy would be clear. Previous studies have attempted to compare costs based on the type of vascular access, but they have typically ignored the pre-dialysis period and have not attempted to deal with selection bias that is likely to occur in this situation. What is needed is to compare costs for patients with an AVF based on when that AVF is placed, to determine if earlier placement is associated with lower costs after adjusting for patient characteristics and selection bias.

Specific Problem

For those who are good candidates for an AVF, the timing of their AVF placement in relation to dialysis initiation can be classified into three distinct groups: (i) those who have had an AVF placed early enough so that it is mature and ready for use when it is time to begin chronic dialysis; (ii) those who have had an AVF placed prior to dialysis initiation that has not had enough time to mature, forcing them to begin dialysis using temporary catheters until the AVF is ready; and (iii) those who do not have an AVF placed until after they have already begun regular dialysis, resulting in the full maturation time occurring while they dialyze with catheters.

The main research question I wish to address is: Does having a mature AVF at the start of dialysis result in a net cost-savings to Medicare compared to either: having an AVF in place but not yet mature at initiation, or having an AVF placed soon after the start of dialysis?

Currently, Medicare makes a few exceptions regarding coverage of ESRD patients for those not already Medicare eligible. While Medicare does not have any exceptions involving AVF

placement prior to dialysis, if doing do would actually result in lower overall costs it might benefit Medicare to make such an exception.

Objectives

In order to address this question, I believe several analyses are required, including:

1. Identifying the three specific groups of patients above and comparing their demographics and disease burden to see what influences the status of their AVF at the time of dialysis initiation.

2. Investigating the total costs to Medicare generated by each patient group, with full consideration given to the fact that costs may be attributable to not only the timing of their AVF placement but also other characteristics of those patient groups (observable as well as unobservable).

3. Estimating how changes in the timing of AVF placement (i.e. changing groups) would affect the costs generated by patients, while taking into account their characteristics which may have influenced the placement timing actually observed.

It is important to note that all three groups (mature AVF at initiation, maturing AVF at initiation, AVF placed after initiation, or "delayed AVF") contain individuals who are deemed candidates for the use of an AVF. This study explores the *timing* of AVF placement for those patients, excluding those who never had an AVF placed.

Background

Chronic Kidney Disease and End Stage Renal Disease

The loss of kidney function is typically a degenerative process that can be brought on by several possible causes ranging from congenital irregularities to acquired medical conditions such as diabetes and hypertension. This progressive kidney loss is generally measured through laboratory values of biochemical markers reflecting how much waste material is present in the blood and urine as well as how quickly that waste is removed from the blood. The longer it takes the kidneys to filter the blood and the less waste they are able to remove, the more severe the

kidney damage. The severity of kidney damage – referred to as Chronic Kidney Disease, or CKD – is classified by these biochemical markers into five stages: 1-3 being "early" or "moderate" CKD, and stages 4 or 5 reflecting "severe" CKD. Kidney damage beyond that equates to the total loss of all kidney function, or End Stage Renal Disease (ESRD). The treatment of ESRD requires either regular dialysis or a kidney transplant. Dialysis is much more common than transplantation, and clinic-provided hemodialysis (HD) is the treatment modality for the majority of patients. Other types of dialysis, such as home-dialysis or peritoneal dialysis (PD), are much less common. According to the most recent estimates, 98% of patients starting renal replacement therapy start with some sort of dialysis, and of those, 93% begin with clinic-provided HD (USRDS, 2010, Table D.1)**.**

Hemodialysis

The process of hemodialysis is typically carried out over three to four hour sessions three days a week. During this process the body's blood is filtered through an external dialysis machine which performs the functions the patient's kidneys are no longer able to do. Blood is pumped from a resting patient's body through a vascular access in the skin, through the dialysis machine and then back into the patient's body. There are two main types of vascular access: catheters and internal accesses. Catheters are plastic tubes that are inserted through the skin directly into a vein. Catheters can be used for dialysis almost immediately, and while they sometimes remain inserted after the dialysis session, they are not intended to be permanent. Internal accesses, either arteriovenous fistulas (AVFs) or arteriovenous grafts (AVGs) are both placed through surgical procedures and once matured remain under the skin. In an AVF, an artery is surgically joined to a vein. This causes increased blood flow into the vein which over time makes it larger and stronger. After a period of time (typically one to six months), the AVF has matured to the point where it is strong enough for dialysis. At this point, needles are inserted through the skin and into the matured vein to access the body's blood. An AVG is similar to an AVF except that instead of directly joining the artery and vein, a synthetic tube is used to connect the two to achieve the same result. Typically, an AVG is done if the patient is too frail or has veins that are too small or weak for an AVF. Just as with an AVF, time is required to allow an AVG to mature, but typically it is only a few weeks. In practice, AVFs are much more common than AVGs, and are becoming even more so. Therefore, most of the clinical literature and research in recent years has focused on AVFs.

Health Insurance for Hemodialysis Patients

All patients with ESRD are eligible for Medicare coverage, but not necessarily right away. For patients not previously eligible for Medicare (i.e. those under age 65), coverage does not begin until 90 days after the start of ESRD. Additionally, for those previously covered by private insurance (typically through their employer), federal law mandates that their insurer must continue to cover them for up to 30 months after the start of ESRD as long as the premiums continue to be paid. Often, however, patients elect to switch over to Medicare prior to the end of those 30 months, either because they receive more benefits from Medicare or because regular dialysis (and the deteriorated health it reflects) makes keeping a job – and paying their private insurance premiums – no longer feasible.

Once Medicare becomes the primary insurance payer, any health encounter produces a bill, or "claim", that is provided to the United States Renal Data System (USRDS) and included in research files. The claims contain information on diagnoses, procedures, and costs, although they typically do not capture important details such as disease severity or whether the patient is prescribed medication. Claims can be used to determine when a particular vascular access is placed because the claim will contain procedure codes from either the Current Procedural Technology (CPT) or the International Classification of Diseases (ICD-9-CM). In addition to claims, at the start of ESRD all patients have medical information collected using the CMS-2728 Medical Evidence Form (Appendix A), which not only includes general demographics and pre-existing conditions, but also the type of vascular access being used at dialysis initiation, which can help identify whether an AVF is mature at the time of dialysis initiation. Any procedures – including the insertion of AVFs – performed prior to the start of Medicare coverage (such as during the first 90 days for those not previously covered by Medicare) are not paid by Medicare and therefore will not produce a Medicare claim.

Medicare claims include the variables needed to process a claim, but clinical information is rarely available. For example, Medicare claims will indicate when a lab test is performed, but the result of that lab test is typically not provided. This means that within Medicare data, laboratory values cannot be used to determine CKD stage. Pharmacy data is also not available from the current Medicare datasets. While Part D coverage began in 2006, datasets are not publically available at the time of this analysis. However, many of the drugs given to dialysis patients are given intravenously (iron, erythropoietin), and therefore are included in the current Medicare datasets. Therefore, lack of prescription drug information should not adversely affect this study.

Reimbursement of Outpatient Dialysis Facilities

While some patients receive hemodialysis in an inpatient hospital or have home hemodialysis machines, the large majority of patients receive their treatment in outpatient dialysis clinics. These dialysis clinics are reimbursed by Medicare through a combination of a base composite rate for most services and separately billable services. While the base composite rate is case-mix adjusted, it is a fixed rate which covers basic dialysis, the usual laboratory tests, and certain supplies used for dialysis. Therefore, it is impossible to examine the "true" cost to providers of dialysis since all sessions at a particular provider are reimbursed at the same rate. Separately billable items include some diagnostic laboratory testing and most injectable drugs, which can be significant. Details of the payment system are available on-line (http://www.cms.hhs.gov/ESRDPayment/, accessed 11/11/10). Since the composite rate ensures that the cost to Medicare of dialysis sessions is relatively consistent, differences in costs will be due to differences in the amount of injectable medications, dialysis complications such as clotting or infections which produce their own claims, and the frequency and intensity of other health issues common in this population including stroke, heart failure, and other events requiring hospitalization.

Selection Bias, Ordered Probit Models and the Heckman Correction

A common problem with data from administrative databases is omitted variable bias. Since the data capture only billing information, often there are specifics – such as severity of disease or patient behavior – which are not captured. When using these data sources to compare treatment groups, this omitted variable issue can produce selection bias. The unmeasured characteristics may influence some patients to either self-select or be selected into one of the treatment groups. Within the context of this project, the unmeasured characteristics may affect whether certain patients are more likely to have a functioning AVF at initiation, as opposed to initiating with a catheter. These characteristics may be health status, behaviors, or personality traits that may either lead to their AVF being placed earlier or to extending their declining kidney function to allow their AVF more time to mature. Obviously one can imagine examples of what these characteristics may be, but any of these types of unmeasured attributes may also affect future costs since they can affect their future health status as well, therein resulting in a correlation between the status of their AVF at initiation and overall costs, which is exactly the "selection bias" issue.

One method for addressing this selection bias is to use an ordered probit extension of the Heckman Correction (Greene, 2008, p882). The ordered probit model assumes that placement in each treatment group (as determined by the timing of their AVF placement and their initial vascular access status) is determined by an unobserved latent variable that is a function of patient and provider characteristics. The ordered probit requires a natural ordering of the dependent variable, which in this case represents the timing of AVF placement, and in turn membership in one of the three groups: (1) those with a mature AVF at initiation, (2) those with an immature AVF at initiation, and (3) those with an AVF placed after initiation. Costs are modeled as a log-linear regression dependent on the AVF status and other characteristics of the patient. As detailed by Greene, the error terms of the ordered probit selection model and log-linear cost model are assumed to be bivariate normal and correlated. The ordered probit selection model produces an estimate that is an extension of the Inverse Mills' Ratio first developed by Heckman, which is included in the cost model to account for the correlation.

Specifically, for each individual, i, there is an observed treatment group, z_i, based on cut-offs relating to an unobserved latent variable $z_i^* = a'w_i + u_i$ where w_i are patient characteristics and u_i is a standard normal error term. For each of the j treatment groups $(j=1,2,3)$, there is a unique cost equation that models observed log(cost), or $y_i = b_j'x_i + e_{ij}$, where x_i is a subset of z_i and each of the e_{ij} terms are normal error terms with variance σ_j^2. One assumes that selection into a particular treatment group is associated with overall log(cost), which means that that u_i and each of the e_{ij} terms are correlated with correlation ρ_j.

Therefore, without accounting for the selection bias, the expected value of y_i is as follows:

$$E[y_i \mid z_i, w_i, x_i] = b_j'x_i + E[e_{ij} \mid z_i = j, w_i] = b_j'x_i + E[e_{ij} \mid u_i]$$

and due to the existence of ρ_j the conditional expectation of e_{ij} is non-zero and therefore if not dealt with will result in biased estimates for the b_j. However, since e_{ij} and u_i are assumed to be distributed as bivariate normal variables, it can be shown that the conditional expectation of e_{ij} is

$$\sigma_j \rho_j \lambda_i$$

where λ_i is an ordered probit extension of the Inverse Mills' Ratio. Once λ_i is estimated from the ordered probit selection model it can be included in the cost model as another regressor, and values for σ_j and ρ_j can be estimated in each cost equation, and with a strong instrument in the selection equation the b_j estimates are no longer biased. More detail on this method is available in Appendix C.

Data Transformations and Heteroskedasticity

It is not surprising that total Medicare costs are skewed, and require a data transformation before they can be modeled as an approximately normally-distributed dependent variable. Methods detailed in previous studies (Manning, 1998; Manning, Mullahy, 2001) are utilized (as described in the Methodology section) to determine that a log-transformation is best for these data. After model fitting, predicted values for log(cost) are retransformed using appropriate smearing methods (Duan 1983) while considering possible heteroskedasticity.

Literature Review

Economic Evaluations in Health Economics

In economic evaluations, healthcare costs represent resources used for a particular treatment, and they are evaluated at their opportunity cost – that is, how much they could have produced in their next most valuable use. How costs are quantified depends greatly on the perspective relevant to the policy question at hand: the payer, the health care provider, the patient, or society as a whole. Costs will obviously include health care resources like medications and durable medical equipment, but can also include other things such as patient and care-giver time (Gold, 1996).

Identifying the relevant costs, however, can be difficult. Finkler (1982) points out that for medical data, “charges” do not always fully reflect “costs”, especially if one means “economic costs”. This is particularly true for dialysis services reimbursed at a base composite rate: the composite rate would be the correct cost from the perspective of the payer, but not from the perspective of the provider. Additionally, a patient perspective would have to include the opportunity cost of their time. Identifying the opportunity cost of a patient’s time can be difficult depending on their employment status before, during, and after the treatment, as well as whether time spent away from work can be thought of as leisure time since they may be ill. Dialysis patients may be working prior to the start of dialysis while they still retain some level of kidney function, but often stop working once the thrice-weekly sessions begin, so a procedure performed before the start of dialysis may have different opportunity costs associated with it compared to the same procedure done once dialysis has begun. Finally, when an intervention affects a person’s health status, it can affect future healthcare costs. Patients whose life has been extended can incur future medical costs, including those unrelated to the original intervention. While it is widely accepted that future medical costs related to the treatment should be included, there is no real consensus

within the literature about whether or not to include *un*related future health expenditures (Weinstein and Stason, 1977; Russell, 1986). It has even been suggested that one should include subsequent consumption (or production) of goods and services after the patient has fully healed in the cost calculation (Meltzer, 1997). However, several authors have argued that the amount and extent to which one should include future unrelated costs depends on the situation (Nyman, 2004) and that it should be up to the analyst to determine (Gold, 1996).

Because the objective of this work is limited to Medicare's payer perspective, billing and reimbursement are deemed to provide the full costs to that payer.

Economic Evaluations in ESRD

A few economic evaluation analyses have been performed on the ESRD population, although many have simply compared overall treatment modalities – HD versus PD or a kidney transplant (Klarman, 1968; Ludbrook, 1981; Roberts, 1980; De Wit, 1998) – as opposed to comparing aspects of care within a single treatment modality like HD.

The evaluations that have been done specifically on HD patients have typically focused on aspects such as the setting where HD is provided (Gonzalez-Perez, 2005) or clinical management of secondary biochemical markers like parathyroid hormone (Garside, 2007). Studies assessing the cost-benefit or cost-utility of the type of vascular access used for HD including Schon (2007), Ortega (2005), Manns (2005), Barama (2003), Wasse (2007), Lee (2002), and NIH/NIDDK (1995) simply compare patients using AVFs to those with catheters (and typically ignore the selection bias issue) instead of comparing the *timing* of the placement of the AVF. Wasse's study used an assessment tool created specifically for kidney disease by Hays (1994) and found a significantly higher quality of life for AVF patients compared to catheter patients at dialysis initiation as in terms of physical energy and emotional and social well-being. However, without accounting for the selection bias it is likely that the estimated differences in quality of life are biased. A recent study in Taiwan (Wu, 2009) investigates the timing of AVF placement and shows lower inpatient costs when it is placed prior to HD initiation compared to placing it afterwards, but again, there was no accounting for potential selection bias.

In addition to correcting for selection bias, consideration needs to be given to the pre-ESRD and transition periods, since it has been shown that CKD patients are likely to die before they ever reach ESRD (Foley, 2005). Even analyses that only include patients who reach ESRD should include some discussion about the pre-ESRD mortality, because placing AVFs prior to ESRD

risks spending money on a procedure that may never be used. Estimates of how often patients with an AVF placed die before reaching ESRD (and the associated costs) are prudent if advocating a policy which encourages the early placement of AVFs.

The issue of which future medical costs to include is of particular interest within the dialysis population since regular dialysis is extremely expensive and ESRD patients have a significant disease burden. As opposed to studies where increased survival *may* produce future health care expenditures, in this population any extended life *will* result in very large health care expenditures. The USRDS (2008, 2010) estimates that ESRD patients cost Medicare around $75,000 per patient per year, compared to around $7,600 for non-ESRD patients. In one analysis (Manns, 2003), the author concluded that even inexpensive interventions that extended the life of dialysis patients may not be cost-effective due to the large cost of dialysis and frequent illness of chronic dialysis patients. For obvious reasons, the results of these types of analyses can be sensitive to survival estimates (Garner, 1987) and the effect of mortality should be considered.

Clinical Aspects of HD and AVFs

For HD patients, the evidence of the clinical superiority of AVFs to catheters and AVGs is overwhelming. The National Kidney Foundation (NKF) states on its website that AVFs should be the first choice "…because [they] generally last longer and have fewer problems such as infections and clotting" (http://www.kidney.org/patients/plu/plu_intro/pluo_9.cfm, accessed December, 2010). The literature on which these recommendations are based is extensive, and shows that compared to catheters (and AVGs), AVFs are associated with lower rates of morbidity, mortality, and infection (Astor, 2005; Perera, 2004; Mehta, 1991; Eggers, 2001; Polkinghorne, 2004; Feldman, 1993; Nassar, 2001; Gulati, 2003; Dhingra, 2001; Xue, 2003; Schlieper, 2008; Woods, 1997; Ishani, 2005; Raithatha, 2010). Additionally, long-term use of catheters can reduce the likelihood that a permanent access can be placed later since catheters can cause vein stenosis (Spinowitz, 1987; Barrett, 1988). Lastly, patients using AVFs tend to have better clinical markers and require lower doses of the typical drug therapies like intravenous iron and erythropoietin (Lopez-Gomez, 2008; Chand, 2008; Goicoechea, 2001).

The NKF and its Disease Outcomes Quality Initiative (K/DOQI) first published guidelines for vascular access in the American Journal for Kidney Disease in 1997, and have since updated those guidelines twice (NKF 2000, 2006). In addition to recommending that AVFs should be the first choice of access, the most recent update in 2006 indicates that an AVF should be placed at least six months before the anticipated start of HD treatments. In an article from 2008,

recommendations from the Society for Vascular Surgery indicate that patients with advanced CKD for whom an AVF is appropriate should have that access placed "as soon as possible" after the evaluation (Sidaway). The Healthy People 2010 initiative seems to echo this sentiment by including an objective for increased use of AVFs in *new* dialysis patients (U.S. DHHS, 2000).

Unfortunately, the use of an AVF is not possible for all patients. Those who are frail or who have small veins may not be able to maintain such an access (Albers, 1994). For some of these patients, AVGs provide a reasonable solution but in reality AVGs are being used less and less frequently (USRDS 2008, Vol II, p.98, Figure 5.26). For the purposes of this analysis, the frequency of use and clinical superiority of AVFs – in addition to the current push for their use by several studies as well as organizations like Fistula First – make them a natural choice for an investigation of the association of placement timing and overall Medicare cost. Some authors believe the K/DOQI guidelines are too general, and should take into consideration patient characteristics. In a 2007 article, O'Hare, et al. argued that a patient's age has a significant influence on whether or not they reach dialysis, and therefore that the current recommendations based solely on the level of renal function are not appropriate. For this analysis, however, I am primarily interested in patients who are candidates for the intervention, so I limit the population to those that have an AVF placed at some point.

Medical Insurance, Reimbursement, and Incentives

Ideally, insurance and reimbursement should not affect the quality of health care given to patients, but several articles demonstrate both theoretically and empirically that they can. Ellis (1990) showed theoretically that the way payments are made and the level of supply-side cost-sharing can influence how much care is given. Empirically, studies have shown that changes to Medicare reimbursement policy have influenced hospital behavior (Zwanziger, 1988) and in turn patient outcomes (Cutler, 1995). Within the specialized population of CKD patients, Sands and Perry (2002) identify financial factors that limit the placement of AVFs, including a lack of funding for pre-ESRD care and financial disincentives inherent in the reimbursement policy. It is possible this project may inform potential policy questions involving whether Medicare should consider covering pre-ESRD care such as AVF insertions. If, in fact, placing them earlier would result in an overall cost reduction for Medicare, it may be in Medicare's best interest to cover the cost of AVF placement prior to ESRD in certain patients. Even if placing them earlier results in only a slight cost reduction for Medicare, the improved quality of life associated with AVFs could suggest that such a policy is warranted.

Data

The primary data source for this analysis is the USRDS database of ESRD patients and their Medicare claims. Specifically, I select the subset of all incident dialysis patients who are aged 67 years or older at the time of dialysis initiation to allow for up to two years of Medicare claims prior to dialysis initiation. Patients who initiated during 2006 are used so that all patients may have up to a year of follow-up. The period of time immediately following dialysis initiation is when adverse events (including death) are most common, due to the large change in lifestyle for the patients and the adjustment of the body to the procedure of dialysis. Therefore, a year of follow-up after dialysis initiation is adequate to assess how costs differ among these three groups of patients before, during and immediately after the transition to dialysis. The database contains demographic information for each patient including their age, race, gender, the date regular dialysis began, a date of death, and information about their insurance coverage prior to the start of dialysis. Also available are Medicare claims which contain diagnoses and procedures for each health encounter the patient experiences. These claims make it possible to identify the placement of a vascular access, complications of an access, visits to specific physician specialties, hospital stays, and acute health events. The information in these databases allows me to identify if patients die or switch to another type of renal replacement therapy (e.g. a kidney transplant) before the end of the first year of dialysis. The cost information on the Medicare claims includes the reimbursement amount that Medicare paid out to providers, which represents the full cost to Medicare for that medical claim. Total Medicare costs from all Medicare claims from one year prior to dialysis initiation up to one year after initiation are used and combined into "total cost". This time period was chosen because while the large majority of costs are incurred after the start of dialysis, patients who have an AVF placed prior to initiation will incur that cost at that time. Additionally, other costs associated with dialysis care may occur prior to and during the transition to dialysis, such as vein mapping or the maintenance or revision of a placed AVF. In addition to data from enrollment and claims, the USRDS database contains information from CMS form 2728, the "Medical Evidence" form that is filed for each patient when they become an ESRD patient. A change to the form in 2005 added information relating to the type of vascular access used at the start of dialysis, and whether an AVF is currently maturing if the patient initiates using a catheter.

Data from the Dartmouth Atlas on the "average reimbursement per Medicare beneficiary" is used (http://www.dartmouthatlas.org/data/topic/subtopic.aspx?scat=1, accessed August, 2010) in the selection and cost models as a geographic adjustment, since utilization and reimbursement rates vary greatly across the country. The patient's county of residence is placed into deciles (called

Geographic decile) based on that data and these dummy variables are used for adjustment in several models.

For one of the analysis extensions the Medicare 5% Random Sample is used to identify patients who have an AVF placed but never reach dialysis, since these patients would not be included in the USRDS database of ESRD patients. The 5% Sample is a standard dataset CMS prepares for researchers, and a full description of its contents is available on-line (http://www.resdac.org/Medicare/data_available.asp). The patients in the 5% Sample are followed to see how many patients with an AVF placed die before ESRD begins, to provide an estimate of the cost AVF placement per patient.

Methodology

This analysis investigates the total Medicare costs of a subgroup of incident hemodialysis patients – that is, patients whose first method of renal replacement therapy is hemodialysis – in 2006 who have an AVF placed at some time during the three years observed, comparing the costs across three cohorts defined by the timing of the placement of their AVF. It employs a database of patients and medical claims from the USRDS database. This analysis examines costs from the payer stance, and does not incorporate measures of quality of life as they are not available from Medicare claims. The population of eligible patients is limited to those who have full Medicare coverage for two years prior to the initiation of hemodialysis as their first treatment for ESRD, thus all patients are age 67 or greater at the time of initiation. As stated above, costs represent total Medicare costs from claims from one year prior to initiation through up to one year after. Patients who die or switch to a different type of renal replacement therapy prior to one year after initiation are included in the analysis, but their costs are censored at the date of death or therapy switch.

The methodology developed for this project has been done so in an attempt to adequately perform the following investigations:

1. To identify three specific groups of HD patients based on the timing of their AVF placement and compare their demographics and disease burden to identify differences;

2. To identify the total cost to Medicare generated by each AVF placement group, and to compare those costs while accounting for differences in characteristics and the possible selection bias associated with each group;

3. To estimate how changes in the timing of AVF placement may affect the total cost using methods that appropriately adjust and account for differences in characteristics and the possible selection bias.

These investigations encourage to two obvious extensions which are necessary to inform practical matters involved with health policy. The first extension is to attempt to identify the events which contribute to the observed cost differences. That is, differences in the rates of events (vascular access related or not) that may help to explain why costs are higher or lower within a particular group. This involves the comparison of rates per time at risk as well as modeling the overall counts using Poisson models. The second extension involves whether it is possible to identify who will be a good AVF candidate long before the start of dialysis. This involves a comparison of those patients in the Delayed AVF group (i.e. those who start with a catheter but have an AVF placed later) with patients in a fourth group: those who start with a catheter but do not have an AVF placed within the first year of followup. If, using markers identified from claims more than a year before dialysis, one can accurately predict who is likely to ultimately receive an AVF, then that may help inform policy suggestions involving patient characteristics which signal someone to be a good candidate for early AVF placement.

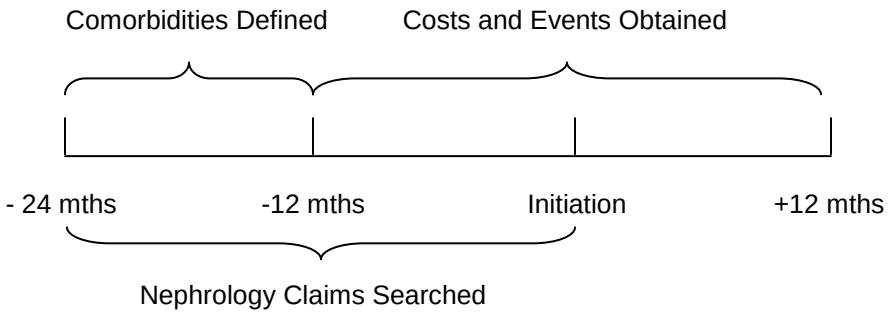
Cohort Construction and Definitions

Using the USRDS database, patients who initiate ESRD in 2006 with HD as their first type of renal replacement therapy at the age of 67 or later have been identified. From these patients, only those who have Medicare Part A and B coverage with Medicare as their primary payer for the entire two years prior to dialysis initiation are included. For those not excluded due to payer status, a combination of claims prior to dialysis initiation and information from CMS form 2728 is used to place patients into three groups defined below.

- Functioning AVF (Group 1): patients are required to have an AVF procedure code from Medicare claims prior to the start of dialysis and to have the 2728 Medical Evidence form indicate that the access used at the first dialysis session was an AVF

- Maturing AVF (Group 2): patients are required to have an AVF procedure code from Medicare claims prior to the start of dialysis and to have the 2728 Medical Evidence form indicate that a maturing AVF is present
- Delayed AVF (Group 3): patients cannot have an AVF (or AVG) code prior to the start of dialysis, but must have one within one year after initiation, and must have the 2728 Medical Evidence form indicate that no maturing AVF (or AVG) is present at initiation.

Comorbidities are defined from claims during the 13 to 24 months prior to dialysis initiation. These comorbidities are defined using the same method the USRDS uses in its annual data report of all dialysis patients. The timing of a nephrologist referral prior to dialysis initiation is obtained from physician specialty code (and date of service) available on Medicare Part B claims. The variable reflecting this timing is calculated as the time from the first recorded nephrologist claim until HD initiation, ranging from 0 to 730 days. Specific codes for AVF procedures, diagnoses, and complications will mirror those identified and used by the USRDS and appear in the Appendix B. The graphic below displays how the data was used to define these variables.



Selection and Cost Models

Costs are obtained from Medicare claims, which include the actual reimbursement amount paid to providers. This allows for exact dollar amounts from the payer prospective. Within the USRDS database, there is an abundance of patient-specific information that can be used for adjustment, including age, gender, race, previous medical history (i.e. pre-ESRD comorbidities, total hospital days, whether a wheelchair is used, etc). Due to the large, positive skew, a transformation of the response variable, total Medicare costs, is warranted. Using the methods detailed by Manning and Mullahy (2001), the large positive skew and heavy tails (kurtosis > 6), calls for a log-transform for the cost data. Since all patients are required to reach ESRD, all patients generate

costs, making it unnecessary to account for zero-dollar amounts in the model. When predicted log(cost) values are transformed back into real dollars, a smearing estimate is employed based on Duan (1983) and Manning (1998). Estimated residuals from the selection-corrected model are used to establish whether there is heteroskedasticity in models on log(cost) by group. A test for heteroskedasticity results in large p-values ($p>0.8$) for the Mature AVF and Maturing AVF groups, indicating little evidence of heteroskedasticity. However, the p-value for the Delayed AVF group is 0.07, indicating that there might be problems with assuming homoskedasticity. Upon closer examination, differences in average residual values are seen across age groups. Therefore, the smearing adjustment is calculated by age group when applied to the Delayed AVF Group.

This study attempts to adjust for unobserved characteristics of the patients and their environments to account for the selection into the type of access for dialysis in two ways. First, all patients who do not ultimately have an AVF placed have been eliminated, to focus on the timing of AVF placement rather than a "catheter vs. AVF" decision by the clinician. Second, an ordered probit extension of the classic Heckman selection correction is used to adjust the cost prediction for unobserved characteristics that affect the placement into the three AVF timing groups, using the STATA "oheckman" routine (Chiburis, 2007).

This ordered probit Heckman correction requires an instrumental variable (IV) to identify the selection bias. The success of this method is dependent on the availability of a good instrument: one that is directly related to group selection but not to overall costs. The IV chosen for this analysis is the timing of a referral to a nephrologist prior to ESRD. Clinically, one would expect that the earlier a patient is seen by a nephrologist, the earlier they are likely to have an AVF placed. At the same time, one would not expect early referral to a nephrologist to be directly related to costs of dialysis treatment, because the bulk of the costs associated with ESRD are incurred after the initiation of dialysis, at which point nearly all patients will be consulting with a nephrologist. This variable is calculated by counting the days between the date of the first Part B claim where the physician specialty indicated on the claim is a nephrologist and the date of dialysis initiation. For patients who do not have a nephrologist claim prior to initiation, the variable is set equal to zero. Although there is no formal test for the appropriateness of a single IV, descriptive data on group assignment and overall cost distributions suggest that this IV may be appropriate for this analysis, as detailed in the Results section.

Much of the cohort construction is performed in SAS (version 9.1), as was some of the survival analysis and mortality rate estimates. However, all of the selection-corrected cost model estimation is done in STATA (version 9.2) using the "oheckman" routine.

Cost Prediction

The selection-corrected cost model includes estimates of an ordered probit Inverse Mills ratio, allowing one to predict what total costs would have been for patients if they had actually been in one of the other groups *while accounting for unobserved characteristics associated with selection into their actual group*. Since models are run on log(cost), the predictions are also done for log(cost), and then converted to dollar scale using a smearing estimate robust to heteroskedasticity, as mentioned above.

Results

Patient Identification

There are a total of 46,511 incident HD patients in 2006 who are aged 67 years or older in the USRDS database. Of those, 15,855 (34%) are excluded because they are identified as not being fee-for-service (FFS) patients with Part A and Part B coverage and Medicare as their primary payer during the entire study period. Table 1 compares demographic information of these excluded patients to those who are FFS with Medicare as their primary payer and shows that they are slightly younger and more often of non-white race. The majority of excluded patients are those enrolled Medicare Advantage for at least some of the study period. Of those remaining, 849 patients are removed who are said to be Fee-For-Service Medicare patients but who have *no* claims during the two-year period, calling into question their insurance status. An additional 159 patients are removed for missing or invalid Medical Evidence form data, resulting in a total of 29,688 patients remaining for assignment into one of the three treatment groups. When the criteria is applied, 3,046 are assigned to the Mature AVF Group (Group 1), 2,381 to the Maturing AVF Group (Group 2), and 6,909 to the Delayed AVF Group (Group 3), producing a final study cohort of 12,336 patients. Those not assigned to any of the three groups include 3,049 patients for whom the Medical Evidence form says they initiated with either a functioning or maturing AVF but who have no Medicare claims for an AVF placement prior to initiation, and 2,787 for whom the Medical Evidence form indicates the presence of an AVG (functioning or maturing) or an "unknown" initial vascular access. A total of 11,516 patients are classified having only a catheter in place at initiation and did not have an AVF placed afterwards. These patients are not included in the study cohort but are used for the extension that compares them to the Delayed AVF patients.

Patient Characteristics

A comparison of the characteristics across the three treatment groups included in the study cohort indicates that they have similar age distributions, but the Mature AVF group tends to be more often male and of Caucasian race (Table 2). The prevalence of comorbidities (as identified from claims during the second year prior to dialysis initiation) are relatively similar, but those in the Maturing AVF group are more likely to have cardiovascular disease, diabetes mellitus (DM) and atherosclerotic heart disease (ASHD) – all conditions relating to or affecting vascular health. Notably, the prevalence of CKD, anemia and hypertension – all associated with kidney function and in reality all likely present to some degree in almost all patients in this cohort – demonstrate a clear difference across the groups. Patients with a mature AVF display the highest prevalence of CKD (87%), compared to 75% for those with a maturing AVF and 55% for those whose AVF placement is delayed until after initiation. Anemia and hypertension reflect similar patterns across the treatment groups (Anemia: 70%, 59%, 47%; HTN: 93%, 90%, 93%). One hypothesis is that the higher demonstrated prevalence of these diseases actually represents earlier *recognition* of kidney disease rather than true prevalence, which could influence whether a patient has an AVF placed prior to starting dialysis. Because of this concern about endogeneity in these variables, they are omitted from both the selection model and the cost models so as to not introduce potential bias into the analysis.

Cognitive impairment and depression, though rare, become more common as you go from the Mature AVF group to the Delayed AVF group, as does the presence of claims involving a wheelchair which may reflect frailty and general health.

Mortality

Since I am measuring total costs as opposed to a rate per time at risk, mortality must be considered. The Maturing AVF and Delayed AVF groups have similar cumulative 12-month mortality, each with about 25% of their population dead a year after initiation (Table 2). In comparison, the Mature AVF group experiences only 17% cumulative mortality at one year, which could reflect better outcomes from the use of the AVF as well as their underlying health status. As it relates to this study, however, a lower mortality rate should actually *increase* costs since living patients produce regular and large medical expenses due to dialysis. Therefore, the lower mortality rate of the Mature AVF group means their total costs are probably higher than they would be if their mortality rate matched that of the other two groups.

While the Maturing AVF and Delayed AVF groups show similar cumulative 12-month mortality, Figure 2 shows that there are significant differences in the *pattern* of mortality rate during the first 12 months. Because the Delayed AVF patients are required to live long enough to have an AVF placed in order to be included in the cohort, there is a selection effect dramatically reducing that group's mortality rate during the first six months. After this point, the relationship between the groups is relatively constant, with the Mature AVF group having the lowest mortality and the Delayed AVF group the highest, as expected. Cox proportional hazards regression in Table 7 shows that older age and presence of disease is typically associated with death. It is likely that given the rates in Figure 2 the proportional hazard assumption is violated, but unadjusted Kaplan-Meier analysis on age groups within each treatment group also suggests that older age is, indeed, associated with mortality (Figures 3a-3c), although neither the Cox model nor the Kaplan-Meier curves are adjusted for selection bias. As a final note, in contrast to the presence of most other diseases, CKD and hypertension in the Cox model have parameter estimates which indicate that they are associated with better survival. This may illustrate how these comorbidities represent early recognition of kidney disease (and in turn better treatment) rather than the actual presence of disease. Because of this potential link with early recognition, which may be associated with unobserved factors influencing AVF placement timing and costs, this finding reinforces the decision to exclude CKD, anemia and hypertension as covariates in the cost analysis.

Unadjusted Cost and Ordinary Least Squares Adjusted Cost

On average, overall costs are lowest in the Mature AVF group and progressively higher in the Maturing AVF and the Delayed AVF groups. The mean cost during the study period for patients in these groups is $103,869, $119,022 and $127,677, respectively (Table 2).

If the selection bias is ignored and Ordinary Least Squares regression is applied to log(cost), statistically significant factors include age, gender, race, and the presence of several comorbidities, including ASHD, cerebrovascular attack (CVA) or "stroke", peripheral vascular disease (PVD), dysrhythmia, cancer, and diabetes (Table 3). In addition, a claim relating to a wheelchair and the average Medicare reimbursement per patient in their geographic region were also significant.

However, as demonstrated previously, the parameter estimates on these factors are likely biased. It is for this reason we pursue the selection corrected cost model.

Ordered Probit Selection Model

For the selection model, an Instrumental Variable (IV) is needed that is associated with selection into the Groups but not overall costs. The timing of the first Nephrologist claim (Number of Days Prior to dialysis initiation, or "NephDays") appears to meet that criteria, based on the data observed. Table 4 shows a clear association between this timing and the treatment group: the earlier a nephrologist is seen, the earlier they are likely to have an AVF placed. At the same time, Figure 1 demonstrates that the distribution of total costs is basically the same regardless of when a nephrologist was first seen. While there is no formal test for the first IV in such a model, these data suggest that the variable NephDays may be an appropriate instrument. It should be noted that this variable is significantly non-Normal and includes differing amounts of values near and equal to zero. For this reason, the two-step method of the "oheckman" procedure is used to fit the model, which is more robust to non-normality (Chiburis, 2007). In addition, several parameterizations of this variable were tested, finding that categorizing the days of nephrology care by deciles produces the best overall model fit.

The significance of NephDays in predicting the timing of AVF placement can be seen in Table 5. Demographics (age, gender, race, geography) are all highly significant, as are many of the comorbidity indicators (ASHD, CHF, DM, GI, Liver Disease) and the frailty measures (a wheelchair claim, log[hospital days], hospitalization indicator variable). To test the assumption that AVF timing is a naturally ordered variable, the use of a multinomial logit model instead of an ordered probit model was tested for model fit and predictive power. It produces results no better than the ordered probit, so the ordered probit model is retained because of its intuitive appeal and its simpler likelihood structure.

Selection-Corrected Cost Model

The cost model (Table 6) shows that presence of comorbidity in most cases is associated with higher costs. Surprisingly, the estimate on age is negative in each group, meaning that after accounting for other factors, older age is associated with lower costs. This is likely related to earlier mortality, since in survival analysis older age is highly predictive of death, as mentioned earlier (Table 7, Figures 3a-3b). There are also possible clinical explanations for why an older patient may cost less: if an 85-year-old is strong enough to reach dialysis, they may actually be healthier in some ways than their 67-year-old counter-part. The unique nature of the dialysis population makes seemingly counterintuitive results not uncommon, even if they are not always fully understood. The parameter estimates on age within the cost model is relatively consistent

across the groups, as is its estimated marginal effect – between $500 and $1,200 of savings for each additional year of age for each treatment group (data not shown).

When used to produce predicted costs, the model does relatively well at predicting average log(cost) for the actual group that a patient belongs to as demonstrated by Figures 4a-4c[1] and an R-squared value of 12.7%.

When patients in one group have costs predicted as if they were in one of the other groups, we obtain the results displayed in Figures 5a-5c. The top figure (5a) represents people actually in the Mature AVF group and displays the predicted cost if they had been in each group. The second figure (5b) represents those actually in the Maturing AVF group and the third (5c) those in the Delayed AVF group. In each case, the predicted distributions for being in the Mature AVF and Delayed AVF groups are relatively stable (although they do shift slightly to the right as you move from 5a to 5c). The distribution of predicted costs for the Maturing AVF group (the middle bar-graph in each case), however, shows the most movement from left to right over Figures 5a to 5c, or as one moves from those actually in the Mature AVF group to the Delayed AVF Group. This appears to be driven by unobservable characteristics of the individuals, as demonstrated by Figures 6a-6c. In these figures, predicted costs are generated without including the Inverse Mills' Ratio, which effectively ignores the impact of the unobservable characteristics. In these predictions, unadjusted for selection, we see little, if any, shifting of the predicted Maturing AVF group costs across actual treatment group cohorts.

As was stated before, while the Mature AVF group demonstrates the lowest actual and predicted cost for all patients, those in the Mature AVF group have the lowest mortality, which actually increases costs. To the extent mortality differences aren't captured by the selection adjustment in the Inverse Mills ratio, estimates of cost savings associated with earlier AVF placement are likely to be a little conservative. However, for completeness the entire process is repeated using only patients who survive for the first 12 months of dialysis. These results are discussed in the section on sensitivity below.

Tables 5 and 6 show that when included in the model, CKD, Anemia, and Hypertension are associated with selection into Groups with earlier AVF placement and lower costs. As stated earlier, it is likely that most, if not all, of patients in the study cohort have some level of kidney

[1] The actual log(cost) graphs have more spread than the predicted log(cost) values due to the fact that the actual values include random error while the predicted values represent those obtained from the fitted model, which do not include random error.

disease regardless of what their Medicare claims show. It is well known within the Nephrology community that recognition of kidney disease has been and continues to be a problem. Most clinicians would agree that the last several years have seen a marked increase in CKD awareness and recognition, but obviously early AVF placement is only possible for patients who have their kidney disease diagnosed and monitored. These data strongly suggest that there is a difference in CKD recognition across the treatment groups. Not only are the comorbidities of CKD and anemia associated with the timing of AVF placement, they are also protective in the survival analysis for mortality after initiation, indicating that they may be surrogates (at least in part) for early detection, continued monitoring and care, and perhaps even unobservable patient characteristics. These results reinforce the decision to exclude these variables from the original analysis.

Sensitivity of Results

The impact of unobservable characteristics on the distribution of costs predicted as if in the Maturing AVF group is consistent when I examine predictions of sub-populations, including age cohorts, those with and without identified CKD, and those who survived 12 months (Figures 7a-7c). This is encouraging since it suggests that cost differences are largely due to factors other than age, survival, or the recognition of declining kidney function. However, the factors that do account for the cost differences are not immediately apparent, and require an extension of the analysis.

Comparison to Ordinary Least Squares Results

The original reason for utilizing a selection-corrected cost model was because it was assumed that selection would introduce bias in OLS models, so it is instructive to compare our results to those that would have been obtained if OLS had been used. Figure 8 displays the mean predicted values for each treatment group as predicted from both OLS and the selection-corrected models. We can see that for each treatment group, the difference between the mean predicted value in the Mature AVF group versus the Delayed AVF group is actually larger in the selection-corrected models than in the OLS models. Therefore, within these data, it appears as though OLS actually underestimates the cost differences associated with the timing of AVF placement.

Extension 1: Adverse event frequency and rates

There may be several drivers of the observed cost differences seen between the treatment groups. Certainly differences in general health status will result in differences in acute event rates, hospitalizations for all causes, as well as the length of each hospital stay. In addition, though, there will be events that are associated directly with the vascular access, such as complication procedures and infections of the vascular access site.

It has been shown in previous research that patients dialyzing with catheters have higher rates of adverse events such as infections and complications (Perera, 2004; Eggers, 2001; Feldman, 1993; Gulati, 2003; Ishani, 2005). An investigation into these events in this cohort shows a similar pattern (Table 8). For simplicity, inpatient hospitalizations are identified and classified by their principal diagnosis code. Table 8 displays unadjusted rates for several types of events before and after dialysis initiation. While it is clear that prior to dialysis initiation there is gradation across the treatment groups for general types of hospitalizations (CHF, ASHD, CVA) it is also clear that the increase in these types of hospitalizations from before to after dialysis initiation – as well as the frequency of vascular access related events after the start of dialysis – show a distinct pattern across treatment groups. Specifically, those who start with a mature AVF have hospitalization rates for infection and complication that are one-half to one-fourth that of patients in the other two groups.

In an attempt to investigate some of observed differences in these events while adjusting for covariates and accounting for selection bias, I employ an endogenous-switching Poisson model using a routine in STATA (Miranda, 2004). Some details of this method are included in Appendix D, but in general the routine fits a Poisson model to the count of events (ignoring the time at risk) while at the same time assessing the extent of the selection bias through an additional "switching" equation to estimate an endogenous treatment variable. Since the STATA routine allows for only two treatment groups, the Maturing AVF and Delayed AVF groups are combined into a single treatment group (the last column of Table 8) and are used as the reference group (for the Mature AVF group) in the endogenous-switching Poisson model results presented in Table 9. This table displays the results of modeling three variables from Table 8: the number of hospitalizations after dialysis initiation for all infections, vascular access infections, and vascular access complications. These variables were chosen due to their direct link to the vascular access. The abbreviated results in Table 9 demonstrate that the Mature AVF group is associated with significantly fewer hospitalizations for each of the infection variables, as evidenced by the negative parameter

associated with the Mature AVF indicator. Additionally, the Mature AVF group tends to have marginally fewer hospitalizations for vascular access complications, although it is not statistically significant. The endogeneity parameter was significant (indicating significant selection) when analyzing hospitalizations for all infection, but not for either of the other two count variables.

Extension 2: Patients who Initiate with a Catheter

A second extension of interest involves an analysis of the Delayed AVF group, and how these patients differ from a group of patients not included in the analysis up to this point: those who initiate with a catheter but do not have an AVF placed within the first year (a "Catheter Only" group). If one could clearly determine differences between these two groups using demographic and disease data from before dialysis was initiated, one could potentially identify patients who will eventually get an AVF and therefore could have it placed earlier – perhaps even prior to dialysis initiation.

Comparing the 6,909 Delayed AVF patients to the 11,516 Catheter Only patients (Table 10) reveals that the latter group tends to be slightly older, more often female, and in general have a higher disease burden and frailty (as identified by claims for a wheelchair). However, a significant portion of this group presents indications that they are not ideal candidates for AVF placement. Almost 75% of the Catheter Only patients are either over the age of 80 or have an indication of significant vascular disease (PVD or CVA) or frailty (a wheelchair claim). While this is also true for the majority of those in the Delayed AVF group (66%), certainly there does not appear to be a large number of Catheter Only patients who could easily be classified as excellent AVF candidates. Additionally, some of those in the Catheter Only group who might be classified as good AVF candidates may simply have not lived long enough to have an AVF placed, as evidenced by the large 1-year mortality observed in that group (56% vs. 25% in the Delayed AVF group). The combination of disease burden and mortality make it unlikely that there are many patients in the Catheter Only group who are clearly good AVF candidates. Perhaps a note of interest involves the timing of the first nephrologist claim: those in the Catheter Only group first saw a nephrologist, on average, even later than those in the Delayed AVF group. In fact, Cox Regression on these two groups indicates that the timing of the first nephrologist claim prior to ESRD is significantly associated with better survival after adjusting for other factors – including treatment group (data not shown). This suggests that regardless of whether an AVF is placed, early referral to a nephrologist may encourage longer survival of patients who initiate dialysis with a catheter.

Discussion

Cost Comparisons

In general, the results reflect much of what would be expected clinically. Patients who have a functioning AVF at initiation represent a healthier and less frail group of patients than those who initiate with a catheter. But it is also clear that placing the AVF early enough so that it has time to mature provides a clear cost reduction over patients whose AVF is still maturing when they begin dialysis.

When coupled with the lower rates of vascular access related complications as well as the previous research demonstrating the improved quality of life for AVF patients, it seems clear that patients who are good candidates should have an AVF placed early enough to assure maturation by the time they initiate dialysis.

Because patients with CKD may die before they ever reach ESRD, it is necessary to consider how that mortality could influence the cost savings of placing AVFs prior to ESRD. Using the 2005 General Medicare 5% Random Sample, it is possible to identify non-ESRD, Medicare-eligible (i.e. age 65 and over) patients who have an AVF insertion and then follow them forward to see what happens to them. This brief analysis identifies about 550 patients in the 5% sample. Within two years of their AVF insertion claim, 71% reach ESRD, 8% die without reaching ESRD, and about 21% survive and remain non-ESRD. While it is difficult to isolate the exact dollar value that represents the cost of an AVF insertion, it is possible to obtain a rough estimate using line-level revenue center information from claims. Data from claims indicates that it is reasonable to assume that an AVF insertion costs Medicare between $1,500 and $2,500. From this information we can calculate the cost per patient who reaches ESRD. If 70% of CKD patients with an AVF inserted reach ESRD, that's a cost of between $2,100 and $3,500 per patient who reaches ESRD. If only 50% reach ESRD, that's a cost of between $3,000 and $5,000 per patient. Given that the average estimated total costs differ by around $10,000 between groups, the pre-ESRD mortality of patients would not appear to negate the cost savings.

If we are to assume that there are about 90,000 new HD patients each year, and that placing AVFs prior to initiation costs between $2,500 and $5,000 per patient who reaches ESRD, that's a total cost of $180M to $450M per year. However, at the average predicted cost savings for a mature AVF at initiation of $10,000 per HD patient, that's a total savings of $900M. Deducting the cost of placing the AVF, we estimate a net savings of between $500M and $800M per year.

Regardless of whether Medicare extends coverage to this type of pre-ESRD treatment or whether health plans and large dialysis providers help to cover this cost, it appears as though the net savings would be significant.

Appropriateness of AVFs and Successful Maturation

Over the last several years, AVFs have received considerable attention within the ESRD and dialysis communities. The advent of the Fistula First program, as well as the increased research surrounding AVFs, has corresponded to an increase in their placement and use as documented above. However, some clinicians have raised the issue of when it is appropriate to place an AVF, and have noted that patient characteristics can often drive the decision surrounding a vascular access. For example, results from a recent survey (Xi, 2010) indicate that nephrologists would prefer that AVF patients are under the age of 65, have minimal comorbidities and no history of a failed access previously attempted. It seems as though clinicians are beginning to push back at the notion that AVFs should be placed in any and all dialysis patients, as is stated in the clinical guidelines. As is always the case, different clinicians will often come to different conclusions regarding the appropriateness of a surgical procedure, especially in a high-risk group.

Additionally, my study is done on an intent-to-treat basis, meaning no consideration is given to what type of vascular access a patient is *actually using* during any particular dialysis session. For example, if an AVF gets clotted or infected, a patient may dialyze using a temporary catheter for a session or two. However, information on the actual access used during a particular dialysis session is not currently available from the Medicare claims, making such a distinction currently impossible. However, from a policy standpoint the intent-to-treat model is appropriate.

The issue of successful maturation of AVFs is also not considered here, even though in reality just because an AVF is placed does not necessarily mean it will mature to the point of use. In a 2006 study by Lok, et al, the authors produced a risk equation for predicting whether an AVF that was placed would actually reach maturity without needing additional procedures or replacement. The four significant variables that increased risk of AVF failure in the risk equation included: age 65 years or older, peripheral vascular disease, coronary artery disease, and non-white race. The authors went on to validate their equation, finding primary failure rates of placed AVFs ranging from 24% in the low-risk group to 69% in the high-risk group. Clearly, age and vascular disease influence the appropriateness of AVFs as well as their potential success. Within the parameters of this study it is impossible from these data to accurately identify if or when an AVF fails.

Along these lines, I recognize that not all patients are ideal candidates for an AVF. Therefore, it is often not simply a matter of placing an AVF sooner – sometimes it is a question of whether or not to place one at all. It is likely that some patients in the study cohort for this thesis would be considered by Lok's risk equation to be in medium or even high risk categories for AVF failure (especially considering their ages), and it may be the case that those who received an AVF later may have done so because their clinician determined that it was the proper course of action to take. Clearly the decision of whether or not to place an AVF (and when) should be done on an individual basis, and clinician autonomy should be respected when recommendations for or against a certain procedure are given. The analyses here have assumed that since an AVF was ultimately placed, it was determined by a clinician that it was appropriate to do so. The results suggest that given that assumption, there appears to be a cost-savings in having a mature AVF in place at the time of dialysis initiation.

Limitations

Clearly those aged 67 years or older at the time of initiation are a specific subset of all incident dialysis patients. These patients are likely to have worse health and a higher disease burden than their younger counterparts. In addition, event rates and overall costs might look very different – after all, as mentioned above, age is a significant factor when clinicians are determining the appropriateness of an AVF. Therefore, the results from this analysis may not be directly generalizable to the entire population of incident dialysis patients. However, while these patients may not be representative of all dialysis patients, they do represent a significant proportion of the HD population and its cost. According to the USRDS, in 2006 there were 101,306 incident HD patients, of which 51,182 (51%) were aged 65 or older (USRDS, 2008). Additionally, of the $20.3 billion Medicare spent on all ESRD patients in 2006, those aged 65 or older accounted for 48% ($9.8B) of that total.

This study also excluded patients who were not FFS with Medicare as their primary payer for the entire study period. The majority of those excluded had Medicare Advantage coverage at some point during the period of interest, and while they still generate Medicare costs, their full claims information is not available, making it impossible to identify those who have an AVF placed.

Table 1. Patients Excluded due to Insurance Status

	Excluded due to Insurance Status*		Included: FFS and Part A/B Eligible		
Total	15,855		30,696		
	N	percent	N	percent	
Age					
Mean	75.9		77.0		
Median	75		77		
67-74	7,332	46.2	11,838	38.6	
75-84	6,957	43.9	14,759	48.1	
85+	1,566	9.9	4,099	13.4	p <.0001
Race					
White	11,100	70.0	23,685	77.2	
African American	3,696	23.3	5,909	19.3	
Other Race	1,059	6.7	1,102	3.6%	p <.0001
Hispanic					
Yes	2,433	15.3	2,348	7.6%	
No	13,299	83.9	28,173	91.8	p <.0001
Gender					
Male	8,674	54.7	16,241	52.9	
Female	7,180	45.3	14,455	47.1	p = .0004
Census Division					
Northeast	3,577	22.6	5,995	19.5	
South	5,056	31.9	11,910	38.8	
Midwest	2,585	16.3	8,060	26.3	
West	4,240	26.7	4,528	14.8	
Other/Unknown	397	2.5	203	0.7	p <.0001

* Patients excluded due to insurance status are those who were not fee-for-service (FFS) and Part A and B eligible with Medicare as their primary payer for the entire study period.

Table 2. Treatment Group Characteristics

	Mature AVF		Maturing AVF		Delayed AVF	
Total	3,046		2,381		6,909	
	N	Percent	N	Percent	N	Percent
Age						
Mean	76.2		76.4		76.5	
Median	76		76		76	
65-74	1,291	42.4	999	42.0	2,819	40.8
75-84	1,443	47.4	1,135	47.7	3,338	48.3
85+	312	10.2	247	10.4	752	10.9
Race						
White	2,485	81.6	1,864	78.3	5,421	78.5
African American	424	13.9	436	18.3	1,260	18.2
Other Race	137	4.5	81	3.4	228	3.3
Gender						
Male	1,951	64.1	1,321	55.5	3,808	55.1
Female	1,095	35.9	1,060	44.5	3,101	44.9
Comorbid Conditions						
ASHD	1,236	40.6	1,102	46.3	2,828	40.9
CHF	914	30.0	835	35.1	2,329	33.7
CVA	385	12.6	344	14.4	933	13.5
PVD	740	24.3	594	24.9	1,579	22.9
Other Cardiac Disease	680	22.3	558	23.4	1,566	22.7
COPD	501	16.4	441	18.5	1,329	19.2
GI	183	6.0	157	6.6	504	7.3
Liver Disease	38	1.2	22	0.9	115	1.7
Dysrhythmia	733	24.1	637	26.8	1,805	26.1
Cancer	401	13.2	299	12.6	814	11.8
Diabetes	1,658	54.4	1,487	62.5	3,821	55.3
Anemia	2,140	70.3	1,408	59.1	3,246	47.0
CKD	2,663	87.4	1,775	74.5	3,767	54.5
Hypertension	2,827	92.8	2,130	89.5	5,744	83.1
Cognitive Impairment	43	1.4	29	1.2	105	1.5
Depression	134	4.4	117	4.9	348	5.0
Uses a Wheelchair	443	14.5	495	20.8	1,689	24.4
Additional Variables						
Nephrology Days (mean)	546.3		459.6		336.4	
Nephrology Days (median)	637		555		315	
Died within one year of ESRD	518	17.0	612	25.7	1,697	24.6
Kidney transplant within one year	41	1.3	14	0.6	13	0.2
Mean days to death (those that died)	174.4		158.5		206.96	
Mean Cost	$103,869		$119,022		$127,677	

See Appendix E for abbreviation definitions.

Table 3. Results from Ordinary Least Squares on log(cost)

	Mature AVF			Maturing AVF			Delayed AVF		
	Coefficient	Std Err	p-value	Coefficient	Std Err	p-value	Coefficient	Std Err	p-value
Age	-0.005	0.002	0.001	-0.010	0.002	0.000	-0.006	0.001	0.000
Female	0.006	0.018	0.734	0.040	0.020	0.052	-0.029	0.011	0.007
Black	0.083	0.025	0.001	0.048	0.026	0.065	0.007	0.014	0.606
Other	0.002	0.041	0.967	0.079	0.055	0.152	-0.060	0.030	0.043
ASHD	0.069	0.019	0.000	0.033	0.023	0.141	0.026	0.013	0.039
CHF	0.024	0.022	0.292	0.023	0.025	0.371	-0.013	0.014	0.344
CVA	0.015	0.026	0.557	0.001	0.029	0.963	0.010	0.016	0.547
PVD	0.075	0.021	0.000	-0.004	0.024	0.883	0.083	0.013	0.000
Other Cardiac Dis.	-0.020	0.023	0.389	0.004	0.026	0.893	0.020	0.014	0.159
COPD	0.038	0.024	0.112	0.012	0.027	0.647	0.024	0.014	0.099
GI	0.056	0.037	0.131	0.036	0.041	0.375	0.015	0.021	0.479
Liver Disease	-0.059	0.077	0.442	0.089	0.107	0.406	0.050	0.041	0.231
Dysrhythmia	0.081	0.022	0.000	0.020	0.025	0.431	0.046	0.014	0.001
Cancer	0.082	0.025	0.001	0.037	0.030	0.217	0.067	0.013	0.000
DM	0.083	0.018	0.000	0.045	0.021	0.035	0.069	0.011	0.000
Uses a Wheelchair	0.131	0.025	0.000	0.096	0.025	0.000	0.135	0.013	0.000
log(total hosp days)	0.015	0.017	0.356	0.026	0.019	0.175	0.013	0.010	0.191
Had at least 1 hosp.	-0.029	0.036	0.425	0.014	0.043	0.749	-0.006	0.024	0.804
Geographic decile 2	0.034	0.047	0.475	-0.035	0.056	0.535	-0.017	0.033	0.610
Geographic decile 3	0.050	0.049	0.308	-0.027	0.057	0.641	0.044	0.033	0.180
Geographic decile 4	0.046	0.046	0.326	-0.044	0.054	0.418	0.015	0.032	0.630
Geographic decile 5	0.069	0.048	0.148	0.025	0.054	0.640	0.069	0.032	0.032
Geographic decile 6	0.097	0.046	0.035	0.037	0.054	0.494	0.085	0.031	0.007
Geographic decile 7	0.112	0.047	0.016	0.058	0.053	0.271	0.097	0.032	0.002
Geographic decile 8	0.120	0.045	0.008	0.064	0.052	0.224	0.108	0.031	0.000
Geographic decile 9	0.207	0.046	0.000	0.181	0.051	0.000	0.198	0.031	0.000
Geographic decile 10	0.240	0.043	0.000	0.186	0.049	0.000	0.196	0.030	0.000
Constant	11.534	0.122	0.000	12.177	0.137	0.000	11.867	0.073	0.000
Measures of Fit									
R-Squared	0.098			0.084			0.097		
Adjusted R-Squared	0.090			0.074			0.094		
Overall F-value	12.140		0.000	7.990		0.000	27.220		0.000

Regerence categories: Male, White Race, Absense of disease, Geographic decile 1

See Appendix E for abbreviation definitions.

Table 4. Timing of the first Nephrologist Visit, by Treatment Group

	Median number of months prior to dialysis initiation	Mean number of months prior to dialysis initiation
Mature AVF	20.7	17
Maturing AVF	17.1	14.2
Delayed AVF	7	9.8

Table 5. Results of Ordered Probit Selection Model (modeling prob of being in 'less desirable' group)

	Base Model		Model with CKD variables	
	Coefficient	p-value	Coefficient	p-value
Nephrology days decile 2	0.8365	0.000	0.7756	0.000
Nephrology days decile 3	0.3392	0.000	0.2384	0.000
Nephrology days decile 4	-0.2824	0.000	-0.3515	0.000
Nephrology days decile 5	-0.491	0.000	-0.4326	0.000
Nephrology days decile 6	-0.6368	0.000	-0.3731	0.000
Nephrology days decile 7	-0.6572	0.000	-0.3779	0.000
Nephrology days decile 8	-0.7846	0.000	-0.4686	0.000
Nephrology days decile 9	-0.8014	0.000	-0.4777	0.000
Nephrology days decile 10	-0.8038	0.000	-0.4677	0.000
Age	0.0034	0.077	0.0056	0.003
Female	0.1259	0.000	0.1579	0.000
African American	0.1146	0.000	0.1333	0.000
Other Race	-0.1021	0.086	-0.0811	0.176
ASHD	0.0401	0.127	0.062	0.019
CHF	0.1066	0.000	0.1335	0.000
CVA	0.0327	0.333	0.0392	0.249
PVD	-0.0358	0.195	-0.0199	0.474
Other Cardiac Dis.	-0.0017	0.954	0.0127	0.676
COPD	0.052	0.093	0.0524	0.093
GI	0.0654	0.161	0.1088	0.020
Liver Disease	0.175	0.082	0.2093	0.038
Dysrhythmia	0.0092	0.749	0.012	0.678
Cancer	-0.0062	0.855	0.041	0.233
Diabetes	-0.0114	0.634	0.0485	0.046
Anemia	-	-	-0.2368	0.000
CKD	-	-	-0.5015	0.000
HTN	-	-	-0.1816	0.000
Uses a wheelchair	0.2448	0.000	0.2384	0.000
log(total hosp days)	0.1105	0.000	0.1203	0.000
Had at least 1 hosp.	-0.1992	0.000	-0.1109	0.026
Geographic decile 2	0.0536	0.414	0.0383	0.563
Geographic decile 3	0.0965	0.149	0.0986	0.145
Geographic decile 4	0.1491	0.019	0.1466	0.023
Geographic decile 5	0.1533	0.018	0.1258	0.054
Geographic decile 6	0.1739	0.006	0.1869	0.004
Geographic decile 7	0.1565	0.013	0.1504	0.018
Geographic decile 8	0.1654	0.007	0.1773	0.004
Geographic decile 9	0.1821	0.003	0.1933	0.002
Geographic decile 10	0.1191	0.045	0.1346	0.025
Cutoff 1	-0.524	0.001	-0.7346	0.000
Cutoff 2	0.0756	0.639	-0.1177	0.472
LR test (Chi-sq)	2,042.39	0.000	2,508.42	0.000
Pseudo R-sq	0.0843		0.1035	

Reference categories: Nephrology days decile 1, Male, White Race, Absence of disease, Geographic decile 1. See Appendix E for abbreviation definitions.

Table 6. Results of Selection-Corrected Cost Models on log(cost)

	Base Model						Model with CKD, HTN, Anemia included					
	Mature AVF		Maturing AVF		Delayed AVF		Mature AVF		Maturing AVF		Delayed AVF	
	Coef	p-value	Coef	p-value	Coef	p-value	Coef	p-value	Coef	p-value	Coef	p-value
Lambda	-0.0179	0.615	0.0268	0.268	-0.0279	0.127	0.0345	0.546	0.0777	0.034	-0.0026	0.925
Age	-0.0049	0.001	-0.0099	0.000	-0.0056	0.000	-0.0049	0.001	-0.0097	0.000	-0.0058	0.000
Female	0.0044	0.810	-0.0365	0.074	-0.0312	0.004	0.0078	0.684	-0.0350	0.097	-0.0339	0.002
African American	0.0814	0.001	0.0509	0.050	0.0060	0.666	0.0845	0.001	0.0595	0.024	0.0055	0.693
Other Race	0.0025	0.950	0.0753	0.169	-0.0572	0.053	-0.0006	0.989	0.0736	0.179	-0.0606	0.040
ASHD	0.0691	0.000	0.0333	0.140	0.0267	0.034	0.0682	0.000	0.0401	0.077	0.0255	0.043
CHF	0.0225	0.315	0.0252	0.317	-0.0134	0.333	0.0278	0.225	0.0289	0.263	-0.0136	0.332
CVA	0.0152	0.560	0.0008	0.978	0.0093	0.562	0.0147	0.575	0.0055	0.846	0.0074	0.646
PVD	0.0757	0.000	-0.0049	0.836	0.0847	0.000	0.0748	0.000	-0.0028	0.905	0.0831	0.000
Other Cardiac Dis.	-0.0193	0.397	0.0016	0.950	0.0209	0.147	-0.0206	0.367	0.0007	0.980	0.0192	0.182
COPD	0.0374	0.119	0.0139	0.603	0.0226	0.116	0.0399	0.097	0.0183	0.494	0.0232	0.107
GI	0.0551	0.133	0.0377	0.354	0.0137	0.519	0.0571	0.123	0.0291	0.478	0.0082	0.703
Liver Disease	-0.0607	0.428	0.0939	0.378	0.0466	0.260	-0.0538	0.486	0.0919	0.388	0.0452	0.275
Dysrhythmia	0.0800	0.000	0.0195	0.428	0.0448	0.001	0.0804	0.000	0.0216	0.380	0.0450	0.001
Cancer	0.0819	0.001	0.0359	0.225	0.0676	0.000	0.0820	0.001	0.0338	0.255	0.0644	0.000
Diabetes	0.0831	0.000	0.0439	0.038	0.0703	0.000	0.0826	0.000	0.0537	0.012	0.0664	0.000
Anemia	-	-	-	-	-	-	0.0129	0.577	0.0546	0.028	0.0312	0.019
CKD	-	-	-	-	-	-	-0.0535	0.157	-0.0955	0.007	-0.0317	0.071
HTN	-	-	-	-	-	-	0.0331	0.340	-0.0815	0.019	0.0273	0.083
Uses a wheelchair	0.1276	0.000	0.1030	0.000	0.1315	0.000	0.1375	0.000	0.1183	0.000	0.1344	0.000
log(total hosp days)	0.0139	0.410	0.0274	0.145	0.0128	0.210	0.0176	0.311	0.0314	0.101	0.0135	0.191
Had at least 1 hosp.	-0.0260	0.480	0.0084	0.845	-0.0032	0.892	-0.0310	0.400	0.0117	0.788	-0.0084	0.722
Geographic decile 2	0.0326	0.489	-0.0322	0.560	-0.0169	0.606	0.0328	0.486	-0.0342	0.536	-0.0181	0.582
Geographic decile 3	0.0479	0.324	-0.0223	0.696	0.0438	0.186	0.0516	0.290	-0.0262	0.645	0.0425	0.199
Geographic decile 4	0.0439	0.343	-0.0396	0.464	0.0145	0.645	0.0458	0.325	-0.0442	0.414	0.0123	0.696
Geographic decile 5	0.0672	0.155	0.0277	0.607	0.0679	0.035	0.0700	0.140	0.0232	0.667	0.0680	0.035
Geographic decile 6	0.0953	0.039	0.0403	0.457	0.0838	0.008	0.0993	0.033	0.0415	0.445	0.0812	0.010
Geographic decile 7	0.1103	0.017	0.0623	0.235	0.0960	0.002	0.1147	0.014	0.0607	0.249	0.0946	0.003
Geographic decile 8	0.1176	0.009	0.0669	0.199	0.1070	0.000	0.1214	0.007	0.0675	0.197	0.1052	0.001
Geographic decile 9	0.2041	0.000	0.1850	0.000	0.1967	0.000	0.2098	0.000	0.1870	0.000	0.1955	0.000
Geographic decile 10	0.2383	0.000	0.1894	0.000	0.1958	0.000	0.2412	0.000	0.1870	0.000	0.1924	0.000
Constant	11.520	0.000	12.167	0.000	11.891	0.000	11.575	0.000	12.258	0.000	11.874	0.000
rho	-0.0392		0.0573		-0.0651		0.0754		0.1646		-0.0061	
sigma	0.4569		0.4682		0.429		0.4573		0.4718		0.4283	

Reference categories: Male, White Race, Absence of disease, Geographic decile 1. See Appendix E for abbreviation definitions.

Table 7. Cox Regression on Mortality after Dialysis Initiation

	All Groups Together		Mature AVF		Maturing AVF		Delayed AVF	
	HR	p-value	HR	p-value	HR	p-value	HR	p-value
Mature AVF	(ref)							
Maturing AVF	1.48	0.000	-	-	-	-	-	-
Delayed AVF	1.26	0.000	-	-	-	-	-	-
Nephrology decile 2	1.14	0.132	2.19	0.043	1.04	0.894	1.11	0.287
Nephrology decile 3	1.17	0.067	2.45	0.003	1.28	0.230	1.07	0.479
Nephrology decile 4	1.26	0.007	1.50	0.103	1.15	0.495	1.29	0.015
Nephrology decile 5	1.15	0.108	1.29	0.278	0.97	0.896	1.25	0.038
Nephrology decile 6	1.02	0.812	1.13	0.596	1.30	0.198	0.89	0.356
Nephrology decile 7	1.00	0.985	1.14	0.588	1.05	0.805	0.97	0.826
Nephrology decile 8	1.16	0.113	1.41	0.128	1.19	0.407	1.12	0.370
Nephrology decile 9	0.96	0.673	0.98	0.939	1.06	0.791	0.98	0.900
Nephrology decile10	1.05	0.635	1.40	0.132	1.08	0.731	0.95	0.675
Age	1.05	0.000	1.05	0.000	1.04	0.000	1.04	0.000
Female	0.99	0.807	0.84	0.091	1.17	0.080	0.98	0.673
Black	0.78	0.000	0.91	0.490	0.73	0.011	0.77	0.000
Other race	0.84	0.135	0.83	0.446	0.63	0.096	0.93	0.627
ASHD	1.13	0.007	1.32	0.006	1.07	0.475	1.09	0.131
CHF	1.28	0.000	1.34	0.009	1.25	0.036	1.27	0.000
CVA	1.04	0.533	1.26	0.064	0.92	0.488	1.02	0.765
PVD	1.19	0.000	1.20	0.068	1.36	0.001	1.11	0.082
Other cardiac dis.	1.11	0.038	1.28	0.025	1.29	0.015	0.99	0.930
COPD	1.22	0.000	1.15	0.242	1.33	0.005	1.20	0.005
GI	0.94	0.433	0.84	0.335	0.87	0.436	1.02	0.811
Liver Dis	1.38	0.027	1.82	0.066	1.99	0.077	1.21	0.283
Dysrhythmia	1.22	0.000	1.05	0.660	1.15	0.161	1.33	0.000
Cancer	1.13	0.037	1.20	0.157	1.02	0.867	1.17	0.033
Diabetes	1.05	0.257	1.12	0.224	0.99	0.888	1.05	0.370
Anemia	0.96	0.339	0.87	0.194	0.89	0.237	1.02	0.787
CKD	0.87	0.016	0.93	0.666	0.73	0.013	0.92	0.235
HTN	0.85	0.006	1.13	0.551	0.95	0.720	0.79	0.002
Uses a Wheelchair	1.32	0.000	1.41	0.003	1.42	0.000	1.26	0.000
log(total hosp days)	1.02	0.546	1.19	0.036	0.95	0.507	1.00	0.992
Had at least 1 hosp.	0.88	0.121	0.64	0.023	1.01	0.945	0.91	0.385

= increases mortality (HR > 1.00 and significant)

= protective (HR < 1.00 and significant)

Reference categories: Nephrology days decile 1, Male, White Race, Absence of disease

Table 8. Unadjusted Cause-Specific Hospitalization Rates (per 100 patient-months)

	Mature AVF	Maturing AVF	Delayed AVF	Maturing/Delayed AVF Together
Before dialysis initiation				
CHF	2.199	3.431	3.675	3.612
ASHD	0.318	0.573	0.755	0.709
CVA	0.235	0.331	0.355	0.349
All Infection	0.98	1.288	1.643	1.552
Other	7.647	10.846	11.635	11.433
After dialysis initiation				
CHF	1.542	2.538	3.031	2.909
ASHD	0.571	0.772	0.709	0.725
CVA	0.51	0.601	0.589	0.592
All Infection	2.894	6.141	7.142	6.894
Vascular access infection	0.372	1.482	1.73	1.668
Septicemia	0.528	0.96	1.219	1.155
Other Infection	1.993	3.699	4.194	4.071
Vascular Access Complication	0.821	1.244	1.161	1.182
Other	10.211	14.657	16.236	15.844

See Appendix E for abbreviation definitions.

Table 9. Endogenous Switching Poisson Model Results for Hospitalization Event Counts

	All infection after initiation		Vascular access infection after initiation		Vascular access complications after initiation	
	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value
Presence of mature AVF	-1.08	0.000	-1.699	0.000	-0.023	0.926
Test of endogeneity in treatment group selection	0.161	0.005	0.163	0.150	-0.122	0.323

Table 10. Characteristics of Delayed AVF group and Catheter Only group

	Delayed AVF		Catheter Only		
Total	6,909		11,516		
	N	Percent	N	Percent	p-value
Age					
65-74	2,819	40.8	3,867	33.6	
75-84	3,338	48.3	5,619	48.8	
85+	752	10.9	2,030	17.6	< 0.0001
Race					
White	5,421	78.5	8,953	77.8	
African American	1,260	18.2	2,215	19.2	
Other Race	228	3.3	348	3.0	0.1699
Gender					
Male	3,808	55.1	5,512	47.9	
Female	3,101	44.9	6,004	52.1	< 0.0001
Comorbid Conditions					
ASHD	2,828	40.9	4,834	42.0	0.1638
CHF	2,329	33.7	4,229	36.7	< 0.0001
CVA	933	13.5	1,844	16.0	< 0.0001
PVD	1,579	22.9	2,922	25.4	.0001
Other Cardiac Dis.	1,566	22.7	2,982	25.9	< 0.0001
COPD	1,329	19.2	2,471	21.5	0.0003
GI	504	7.3	877	7.6	0.4236
Liver Disease	115	1.7	217	1.9	0.2775
Dysrhythmia	1,805	26.1	3,397	29.5	< 0.0001
Cancer	814	11.8	1,592	13.8	< 0.0001
Diabetes	3,821	55.3	6,008	52.2	< 0.0001
Anemia	3,246	47.0	5,479	47.6	0.4335
CKD	3,767	54.5	5,693	49.4	< 0.0001
Hypertension	5,744	83.1	9,312	80.9	0.0001
Uses a Wheelchair	1,689	24.4	3,192	27.7	< 0.0001
Additional Variables					
Nephrology Days (mean)	336.4		307.4		< 0.0001
Nephrology Days (median)	315		244		
Died within one yr of ESRD	1,697	24.6	6,392	55.5	< 0.0001

See Appendix E for abbreviation definitions.

Figure 1. Log(Cost) by Timing of first Nephrologist Claim, all Treatment Groups

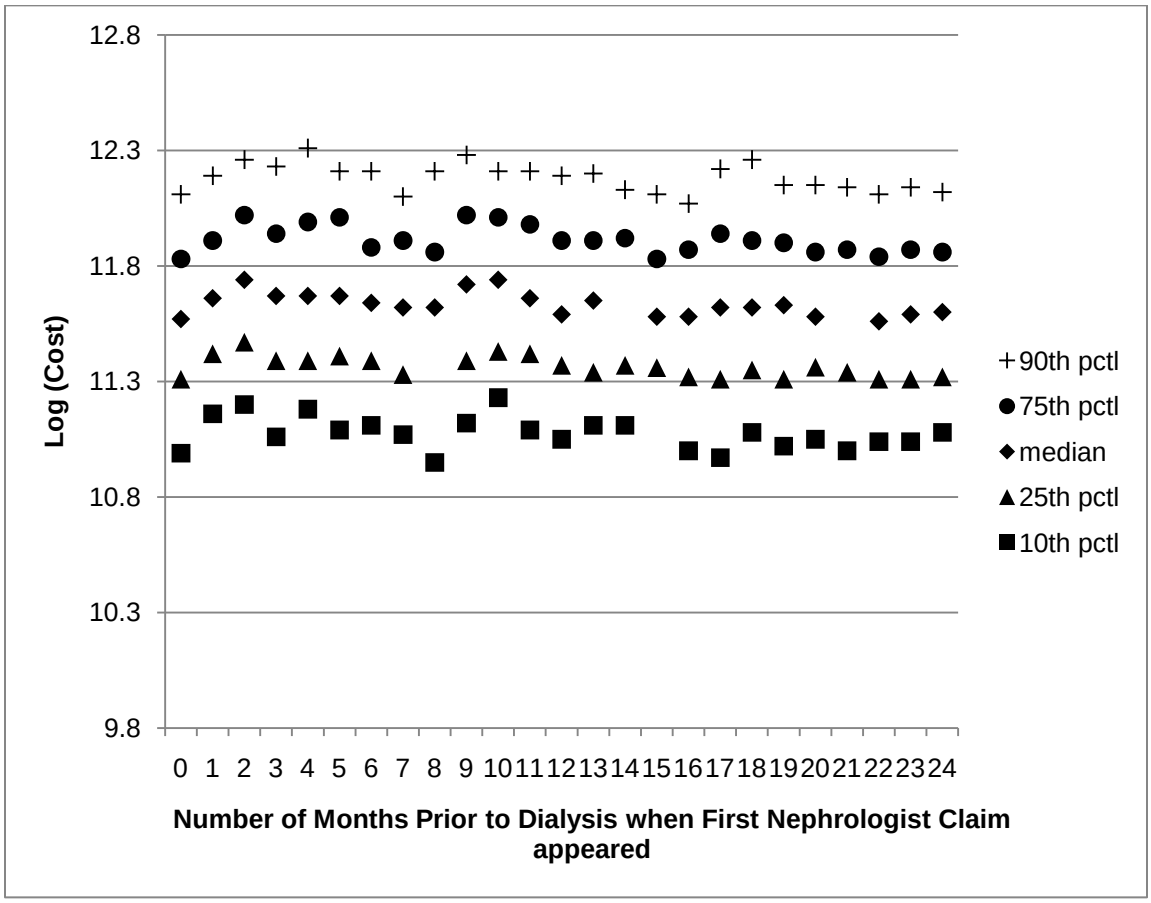


Figure 2. Unadjusted Mortality Rate by Treatment Group

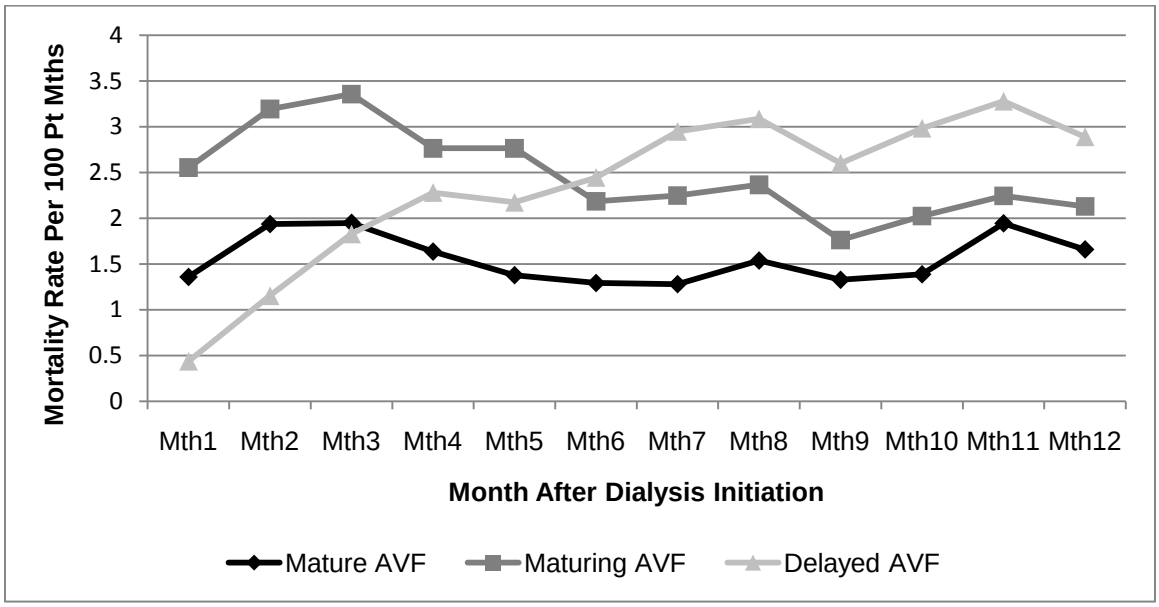
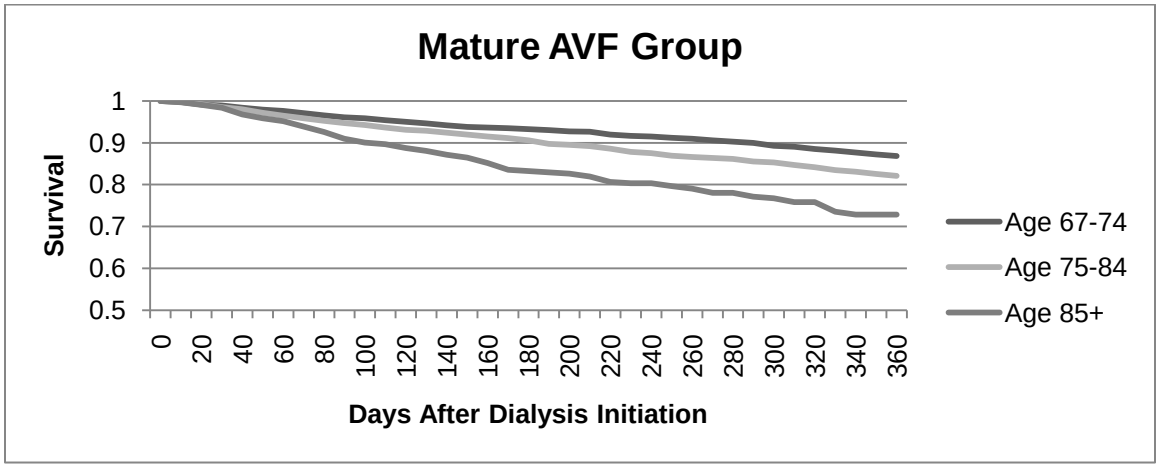
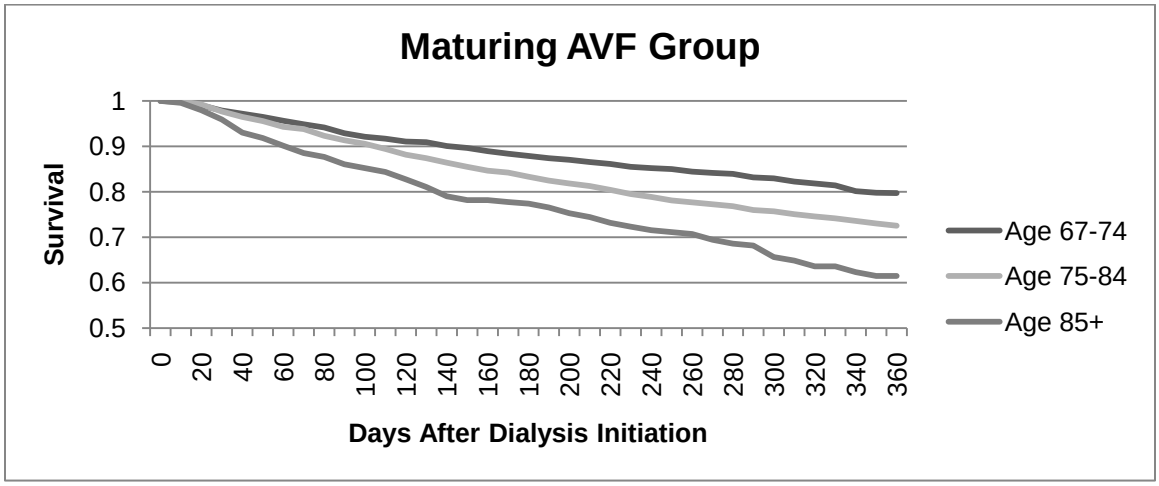


Figure 3a-3c. Kaplan-Meier Survival Curves by Age and Treatment Group





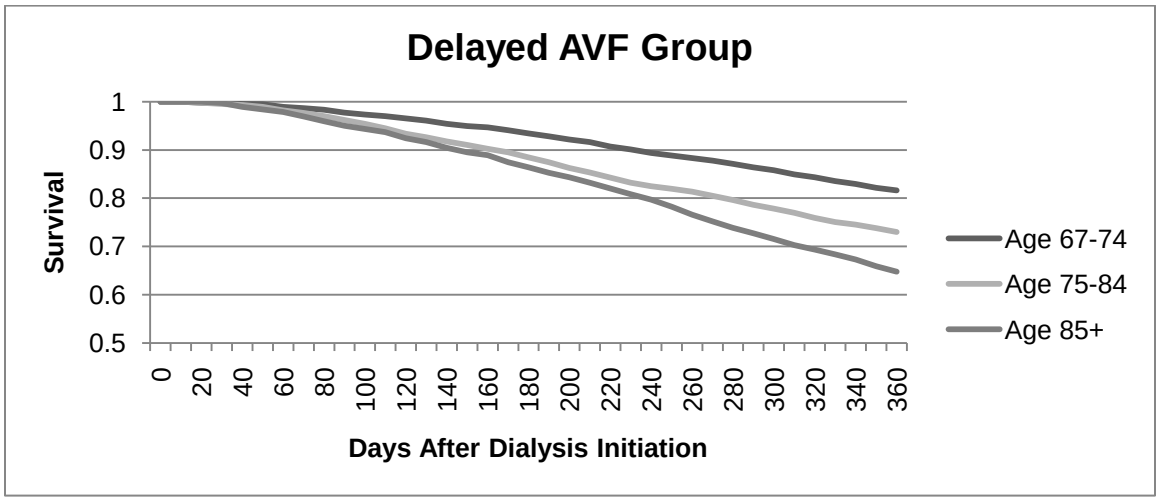


Figure 4a-4c. Predicted log(cost) vs. Actual log(cost), by Treatment Group

Figure 4a. Mature AVF Group

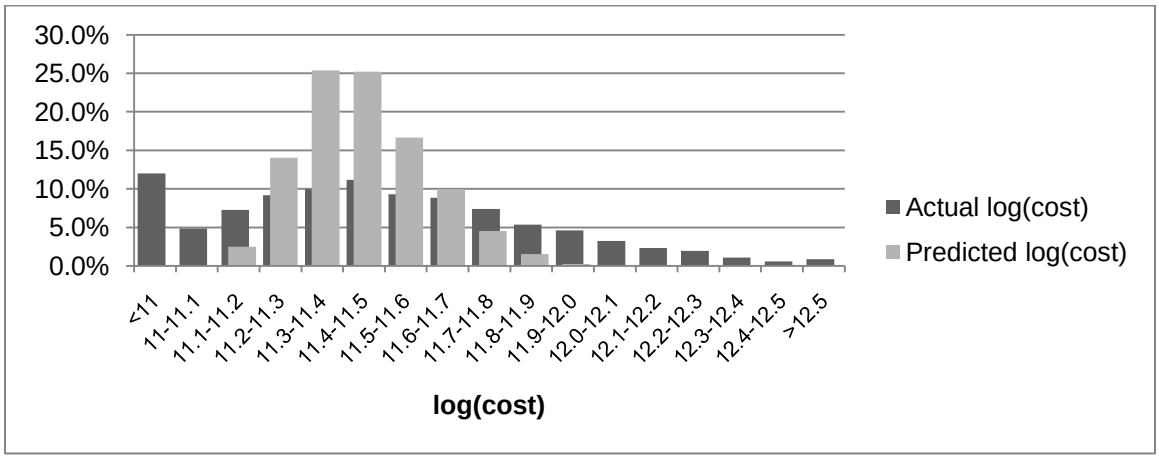


Figure 4b. Maturing AVF Group

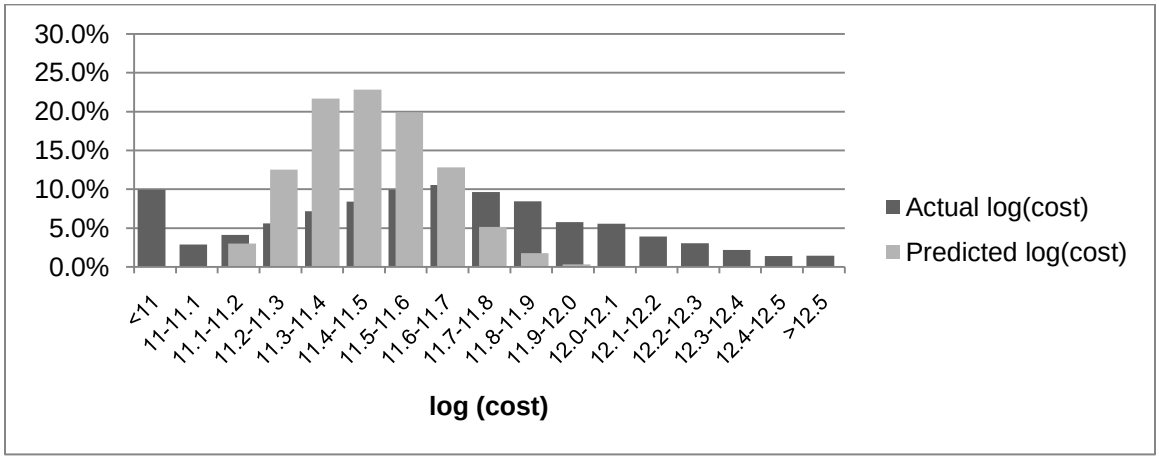
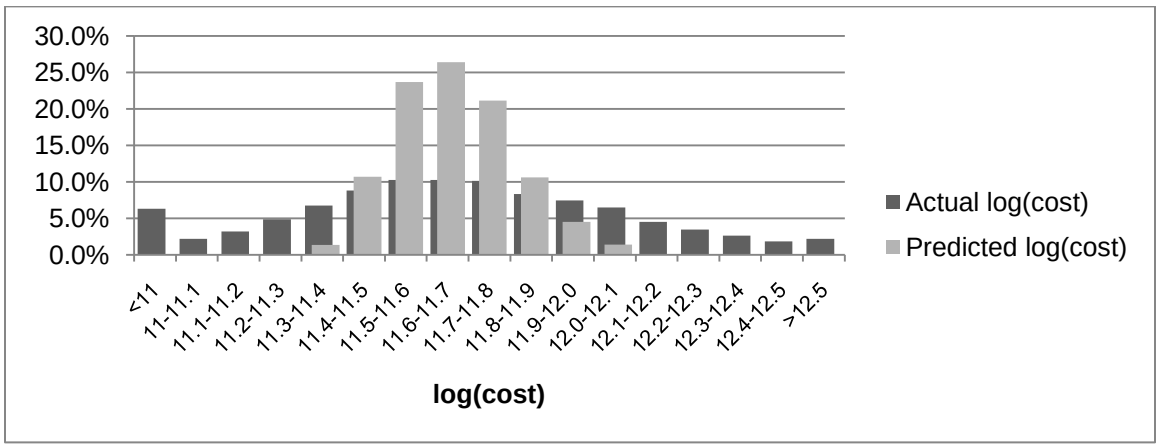


Figure 4c. Delayed AVF Group



Figures 5a – 5c. Predicted cost by Actual Treatment Group

Figure 5a. Those actually in Mature AVF Group, Predicted Costs by treatment group

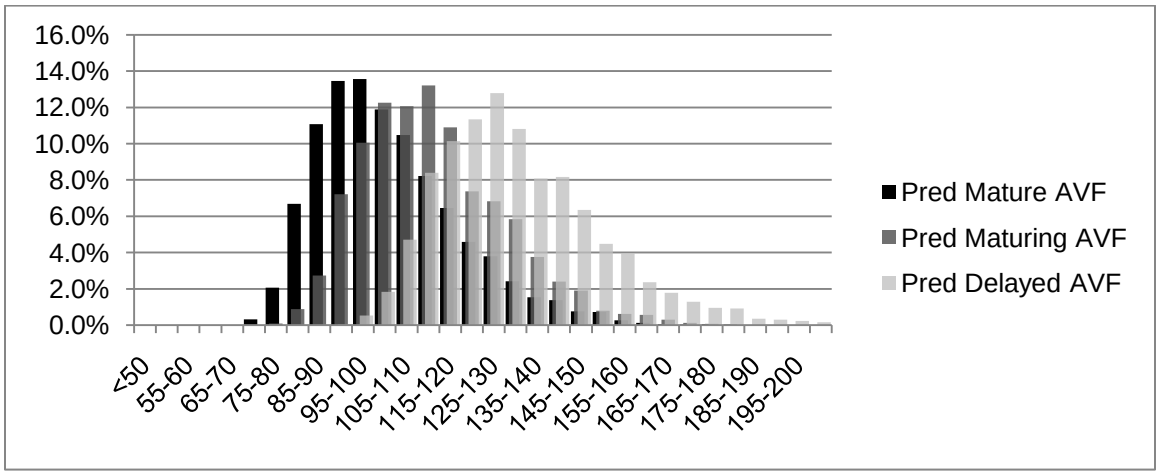


Figure 5b. Those actually in Maturing AVF Group, Predicted Costs by treatment group

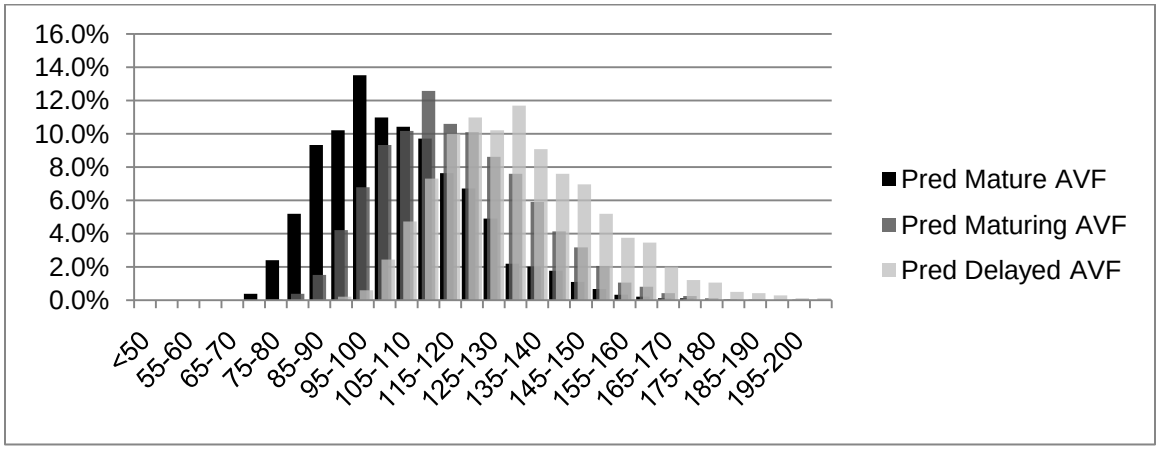
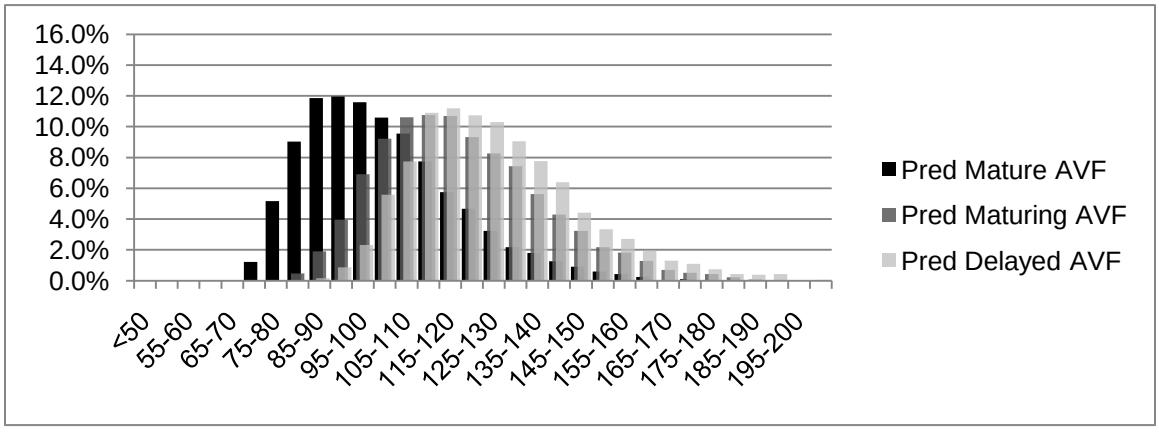


Figure 5c. Those actually in Delayed AVF Group, Predicted Costs by treatment group



Figures 6a – 6c. Predicted Cost by Actual Treatment Group, without Mills Ratio correction

Figure 6a. Those actually in Mature AVF Group

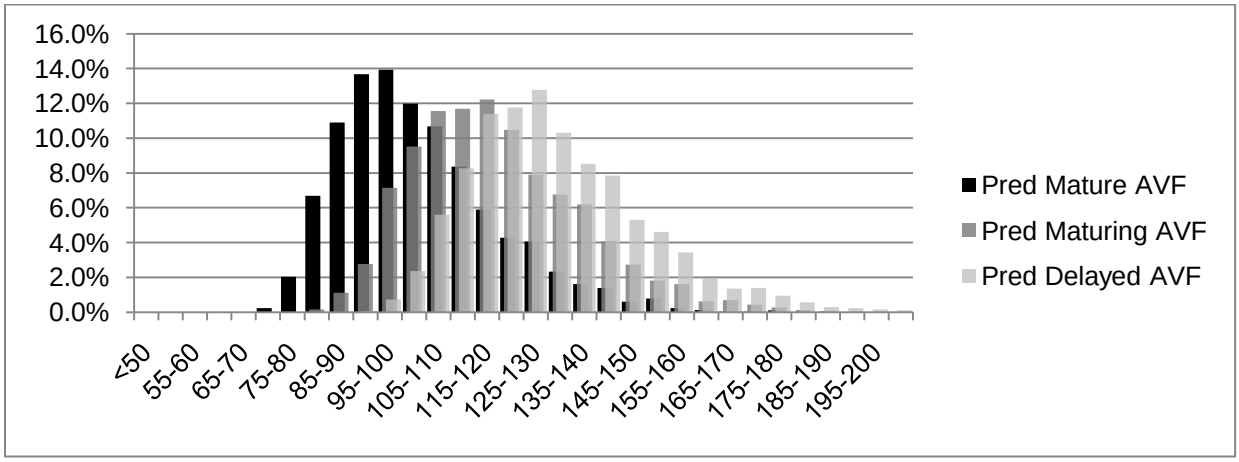


Figure 6b. Those actually in Maturing AVF Group

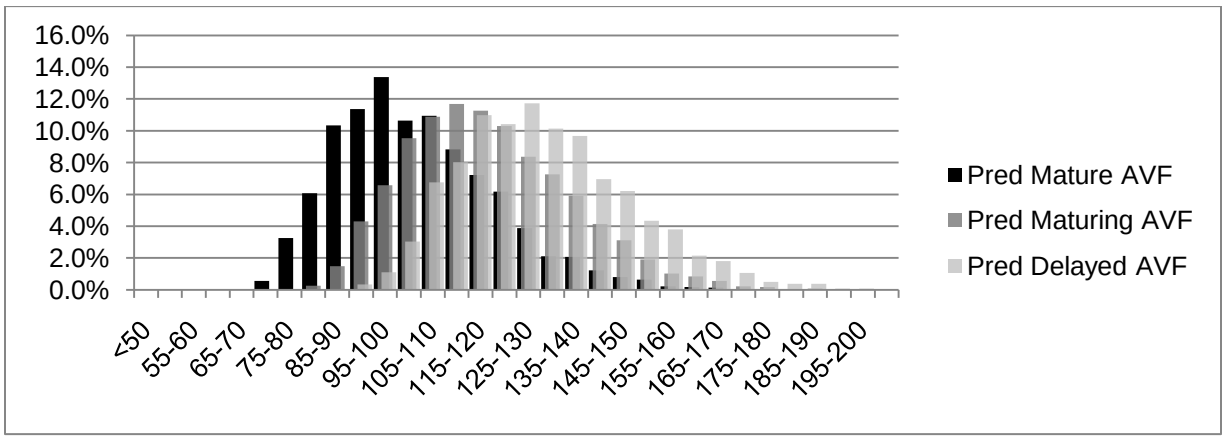
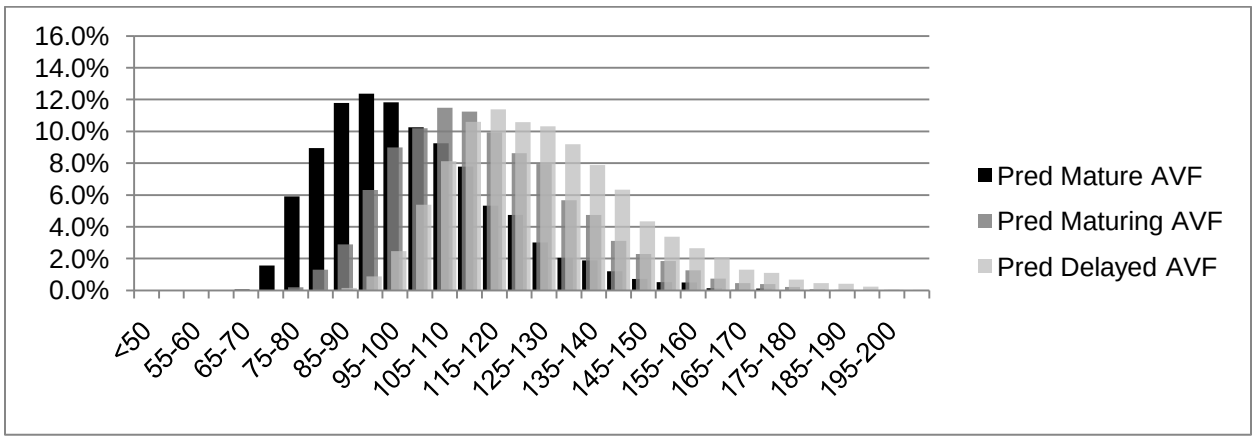


Figure 6c. Those actually in Delayed AVF Group



Figures 7a-7c. Predicted Cost by Actual Group for those who survive on HD for 12 Months

Figure 7a. Those actually in Mature AVF Group

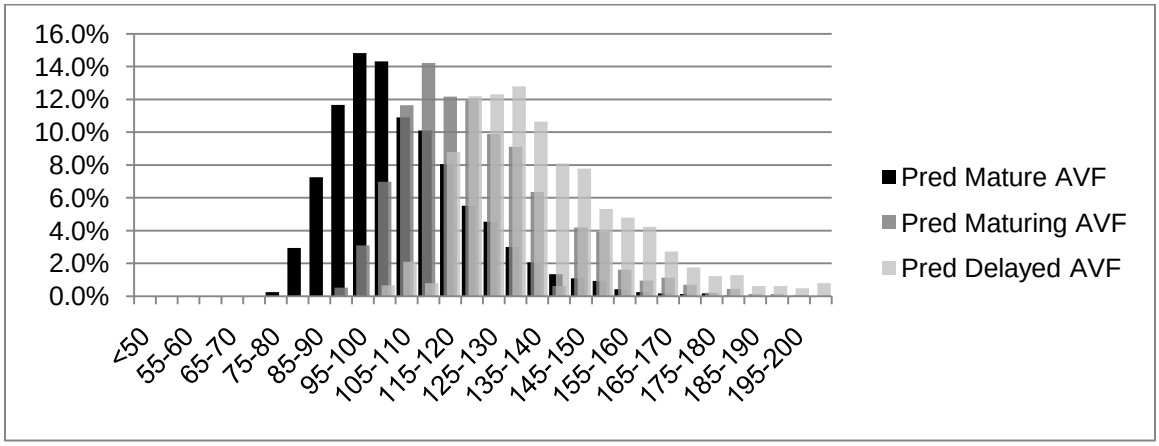


Figure 7b. Those actually in Maturing AVF Group

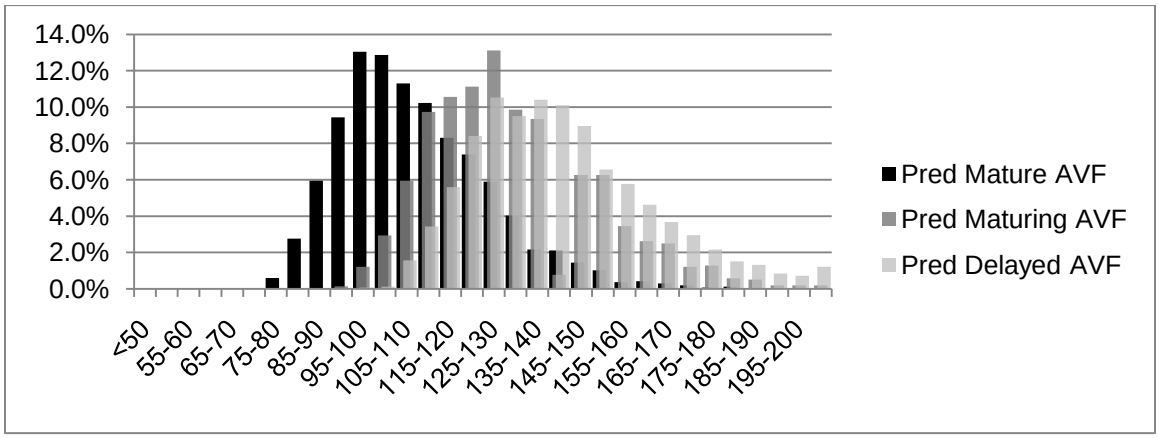


Figure 7c. Those actually in Delayed AVF Group

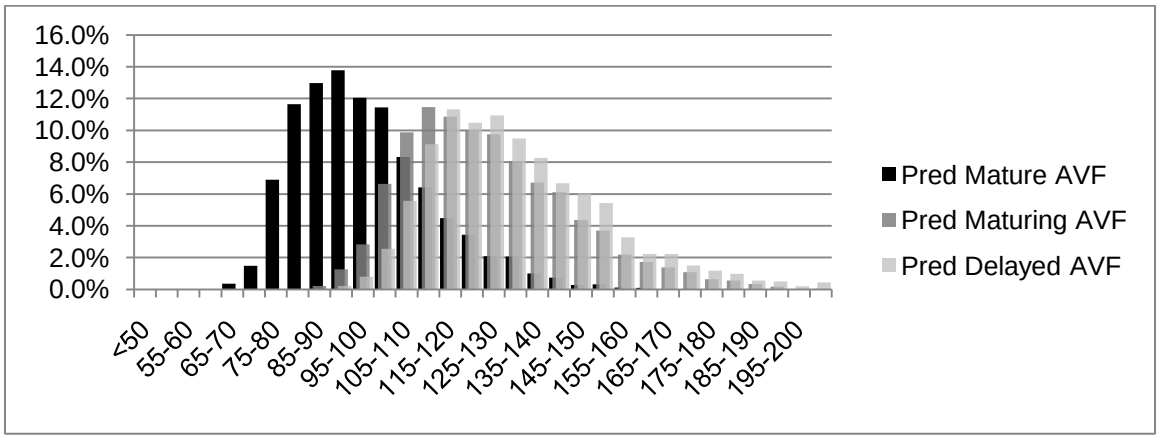
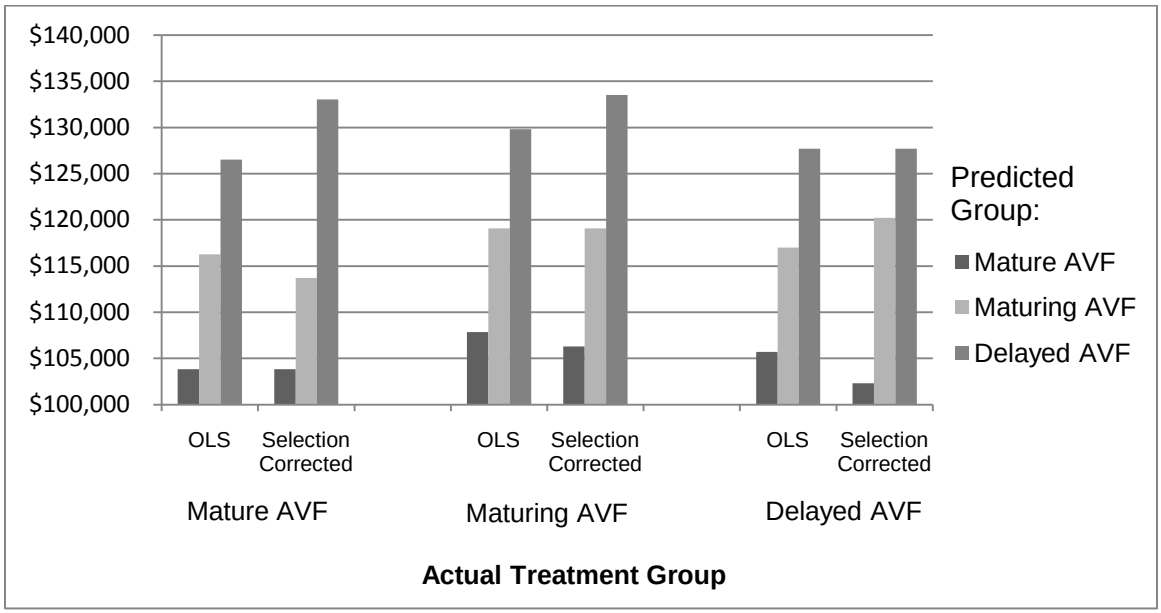


Figure 8. Mean Predicted Cost from OLS vs. Selection-Corrected Models



Bibliography

Abdullah BJ, Mohammad N, Sangkar JV, et al: “Incidence of upper limb venous thrombosis associated with peripherally inserted central catheters (PICC).” Br J Radiol 78:596-600, 2005

Albers FJ: “Causes of hemodialysis access failure.” Adv Ren Replace Ther 1:107-118, 1994

Astor BC, Eustace JA, Powe NR, Klag MJ, Fink NE, Coresh J: “Type of vascular access and survival among incident hemodialysis patients: The Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study.” J Am Soc Nephrol 16:1449-1455, 2005.

Barama AA. “Evaluating the impact of an aggressive strategy to create wrist arterio-venous fistula in patients on hemodialysis.” J Vasc Access. 2003 Oct-Dec;4(4):140-5.

Barrett N, Spencer S, McIvor J, Brown EA: “Subclavian stenosis: A major complication of subclavian dialysis catheters.” Nephrol Dial Transplant 3:423-425, 1988

Chand DH, Teo BW, Fatica RA, Brier M; Medical Review Board of The Renal Network, Inc. “Influence of vascular access type on outcome measures in patients on maintenance hemodialysis.” Nephron Clin Pract. 2008;108(2):c91-8. Epub 2008 Jan 22.

Chiburis R, Lokshin M. “Maximum likelihood and two-step estimation of an ordered-probit selection model.” The Stata Journal (2007), 7, Number 2, pp 167-182.

The Cost Effectiveness of Alternative Types of Vascular access and the Economic Cost of ESRD. Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1995, pp 139-157

Cutler DM. “The incidence of adverse medical outcomes under prospective payment.” Econometrica. 1995 Jan; 63(1):29-50.

de Wit GA, Ramsteijn PG, de Charro FT. “Economic evaluation of end stage renal disease treatment.” Health Policy. 1998 Jun;44(3):215-32.

Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK: “Type of vascular access and mortality in U.S. hemodialysis patients.” Kidney Int 60:1443-1451, 2001

Duan, Naihua: “Smearing Estimate: A Nonparametric Retransformation Method.” Journal of the American Statistical Association 78 (383):605-610, 1983.

Eggers P, Milam R: Trends in vascular access procedures and expenditures in Medicare’s ESRD program, in Henry ML (ed): Vascular Access for Hemodialysis-VII. Chicago, IL, Gore, 2001, pp 133-143.

Feldman HI, Held PJ, Hutchinson JT, Stoiber E, Hartigan MF, Berlin JA: “Hemodialysis vascular access morbidity in the United States.” Kidney Int 43:1091-1096, 1993

Finkler, S. “The Distinction between Cost and Charges,” Annals of Internal Medicine vol. 96, 1982, pp. 102-109.

Foley RN, Murray AM, Li S, Herzog CA, McBean AM, Eggers PW, Collins AJ. “Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999.” J Am Soc Nephrol. 2005 Feb;16(2):489-95.

Garside R, Pitt M, Anderson R, Mealing S, D'Souza R, Stein K. “The cost-utility of cinacalcet in addition to standard care compared to standard care alone for secondary hyperparathyroidism in end-stage renal disease: a UK perspective.” Nephrol Dial Transplant. 2007 May;22(5):1428-36. Epub 2007 Feb 17.

Garner TI, Dardis R. “Cost-effectiveness analysis of end-stage renal disease treatments.” Medical Care 1987;25:25–34.

Gilbertson DT, Liu J, Xue JL, Louis TA, Solid CA, Ebben JP, Collins AJ. “Projecting the number of patients with end-stage renal disease in the United States to the year 2015.” J Am Soc Nephrol. 2005 Dec; 16(12):3736-41.

Gold, Marthe R., Joanna E. Siegel, Louise B. Russell, and Milton C. Weinstein. Cost-Effectiveness in Health and Medicine. New York: Oxford U Press, 1996.

Goicoechea M, Caramelo C, Rodriguez P, Verde E, Gruss E, Albalate M, Ortiz A, Casado S, Valderrábano F. “Role of type of vascular access in erythropoietin and intravenous iron requirements in haemodialysis.” Nephrol Dial Transplant. 2001 Nov;16(11):2188-93.

Gonzalez-Perez JG, Vale L, Stearns SC, Wordsworth S. “Hemodialysis for end-stage renal disease: a cost-effectiveness analysis of treatment-options.” Int J Technol Assess Health Care. 2005 Winter;21(1):32-9.

Greene, WH. Econometric Analysis (6th Ed). Pearson Prentice Hall, 2008.

Gulati S, Sahu KM, Avula S, Sharma RK, Ayyagiri A, Pandey CM: “Role of vascular access as a risk factor for infections in hemodialysis.” Ren Fail 25:967-973, 2003

Hays RD, Kallich JD, Mapes DL, Coons SJ, Carter WB: “Development of the kidney disease quality of life (KDQOL) instrument.” Qual Life Res 3:329-338, 1994

Ishani A, Collins AJ, Herzog CA, Foley RN. “Septicemia, access and cardiovascular disease in dialysis patients: the USRDS Wave 2 study.” Kidney Int. 2005 Jul;68(1):311-8.

Klarman HF, Francis JO, Rosenthal CD. “Cost-effectiveness analysis applied to the treatment of chronic renal diseases.” Medical Care 1968;6:48–54.

Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C. “Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access.” Am J Kidney Dis. 2002 Sep;40(3):611-22.

Lok CE, Allon M, Moist L, Oliver M, Shah H, Zimmerman D. “Risk equation determining unsuccessful cannulation events and failure to maturation in arteriovenous fistulas.” J Am Soc Nephrol. 2006; 17: 3204-3212.

López-Gómez JM, Portolés JM, Aljama P. “Factors that condition the response to erythropoietin in patients on hemodialysis and their relation to mortality.” Kidney Int Suppl. 2008 Dec;(111):S75-81.

Ludbrook A. “A cost-effectiveness analysis of the treatment of chronic renal failure.” Applied Economics 1981;13:337–50.

Manning WG. “The logged dependent variable, heterscedasticity, and the retransform problem.” Journal of Health Economics; 17 (1998): 283-295.

Manning WG, Mullahy J. “Estimating log models: to transform or not to transform?” Journal of Health Economics; 20 (2001): 461-494.

Manns B, Meltzer D, Taub K, Donaldson C. “Illustrating the impact of including future costs in economic evaluations: an application to end-stage renal disease care.” Health Econ. 2003 Nov;12(11):949-58.

Manns B, Tonelli M, Yilmaz S, Lee H, Laupland K, Klarenbach S, Radkevich V, Murphy B. “Establishment and maintenance of vascular access in incident hemodialysis patients: a prospective cost analysis.” J Am Soc Nephrol. 2005 Jan;16(1):201-9. Epub 2004 Nov 24.

Mehta S: Statistical summary of clinical results of vascular access procedures for haemodialysis, in Sommer BG, Henry ML (eds): Vascular Access for Hemodialysis-II (ed 2). Chicago, IL, Gore, 1991, pp 145-157

Meltzer, David. “Accounting for Future Costs in Medical Cost-Effectiveness Analysis,” Journal of Health Economics vol. 16, no. 1, February 1997, pp. 33-64.

Miranda, Alfonso. “FIML estimation of an endogenous switching model for count data,” The Stata Journal (2004), 4, Number 1, pp. 40-49.

Nassar GM, Ayus JC: “Infectious complications of the hemodialysis access.” Kidney Int 60:1-13, 2001

National Kidney Foundation: DOQI Clinical Practice Guidelines for Vascular Access. Am J Kidney Dis 30:S150-S191, 1997 (suppl 3)

National Kidney Foundation. K/DOQI clinical practice guidelines for vascular access update 2000: Am J Kidney Dis 37:S137-S181, 2001.

National Kidney Foundation. K/DOQI Clinical Practice Guidelines and Clinical Practice Recommendations, 2006 Updates, Hemodialysis Adequacy, Peritoneal Dialysis Adequacy, Vascular Access
http://www.kidney.org/PROFESSIONALS/kdoqi/guideline_upHD_PD_VA/va_guide1.htm

Nyman, John A. "Should the Consumption of Survivors Be Included as a Cost in Cost-Utility Analysis?" Health Economics vol. 13, 2004, pp. 417-427.

O'Hare AM, et al.: "When to refer patients with CKD for vascular access surgery: Should age be a consideration?" Kidney Int. 2007 Mar;71(6):555-61.

Ortega T, Ortega F, Diaz-Corte C, Rebollo P, Ma Baltar J, Alvarez-Grande J. "The timely construction of arteriovenous fistulae: a key to reducing morbidity and mortality and to improving cost management." Nephrol Dial Transplant. 2005 Mar;20(3):598-603. Epub 2005 Jan 12.

Perera GB, Mueller MP, Kubaska SM, Wilson SE, Lawrence PF, Fujitani RM: "Superiority of autogenous arteriovenous hemodialysis access: Maintenance of function with fewer secondary interventions." Ann Vasc Surg 18:66- 73, 2004

Polkinghorne KR, McDonald SP, Atkins RC, Kerr PG: "Vascular access and all-cause mortality: A propensity score analysis." J Am Soc Nephrol 15:477-486, 2004

Raithatha A, McKane W, Kendray D, Evans C: "Catheter access for hemodialysis defines higher mortality in late-presenting dialysis patients." Ren Fail. 2010;32(10):1183-8.

Roberts SD, Maxwell DR, Gross TL. "Cost-effective care of end-stage renal disease: a billion dollar question." Annals of Internal Medicine 1980;92(1):243–8.

Russell, Louise B. Is Prevention Better Than Cure? Brookings Institution Press, 1986

Sands J, Perry M. "Where are all the AV Fistulas?" Semin Dial. 2002 May-Jun; 15(3): 146-8.

Schlieper G, Krüger T, Djuric Z, Damjanovic T, Markovic N, Schurgers LJ, Brandenburg VM, Westenfeld R, Dimkovic S, Ketteler M, Grootendorst DC, Dekker FW, Floege J, Dimkovic N. "Vascular access calcification predicts mortality in hemodialysis patients." Kidney Int. 2008 Dec;74(12):1582-7. Epub 2008 Sep 17.

Schon, Donald, et al. “Increasing the Use of AVFs in HD: Economic Benefits and Economic Barriers” Clin J Am Soc Nephrol, 2007; (2) 268-276.

Sidaway AN, et al.: “The Society for Vascular Surgery: clinical practice guidelines for the surgical placement and maintenance of arteriovenous hemodialysis access.” J Vasc Surg. 2008 Nov;48(5 Suppl):2S-25S. Review.

Spinowitz BS, Galler M, Golden RA, et al: “Subclavian vein stenosis as a complication of subclavian catheterization for hemodialysis.” Arch Intern Med 147:305-307, 1987

U.S. Department of Health and Human Services. Healthy People 2010. 2nd ed. With Understanding and Improving Health and Objectives for Improving Health. 2 vols. Washington, DC: U.S. Government Printing Office, November 2000

U.S. Renal Data System, USRDS 2008 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2008.

U.S. Renal Data System, USRDS 2010 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2010.

Wasse H, Kutner N, Zhang R, Huang Y. “Association of initial hemodialysis vascular access with patient-reported health status and quality of life.” Clin J Am Soc Nephrol. 2007 Jul;2(4):708-14. Epub 2007 May 18.

Weinstein, Milton C. and William B. Stason. “Foundations of Cost-Effectiveness Analysis for Health and Medical Practices,” New England Journal of Medicine vol. 296, no. 13, March 31, 1977, pp. 716-721.

Woods JD, Port FK: “The impact of vascular access for haemodialysis on patient morbidity and mortality.” Nephrol Dial Transplant 12:657-659, 1997

Wu LC, Lin MY, Hsieh CC, Chiu HC, Mau LW, Chiu YW, Chen HC, Hwang SJ: “Planned Creation of Vascular Access Saves Medical Expenses for Incident Dialysis Patients.” Kaohsiung J Med Sci 2009; 25:521-9

Xi W, MacNab J, Lok CE, Lee TC, Maya ID, Mokrzycki MH, Moist LM. “Who should be referred for a fistula? A survey of nephrologists.” Nephrol Dial Transplant. 2010; 25(8): 2644-2651.

Xue JL, Dahl D, Ebben JP, Collins AJ: “The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients.” Am J Kidney Dis 42:1013-1019, 2003.

Zwanziger J, Melnick GA. “The effects of hospital competition and the Medicare PPS program on hospital cost behavior in California.” J Health Econ. 1988 Dec; 7(4):301-20.

Appendix A. CMS 2728 Medical Evidence Form

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR MEDICARE & MEDICAID SERVICES

Form Approved
OMB No. 0938-0046

END STAGE RENAL DISEASE MEDICAL EVIDENCE REPORT
MEDICARE ENTITLEMENT AND/OR PATIENT REGISTRATION

A. COMPLETE FOR ALL ESRD PATIENTS *Check one:* ☐ Initial ☐ Re-entitlement ☐ Supplemental

1. Name *(Last, First, Middle Initial)*

2. Medicare Claim Number | 3. Social Security Number | 4. Date of Birth ____/____/____ MM DD YYYY

5. Patient Mailing Address *(Include City, State and Zip)* | 6. Phone Number ( )

7. Sex ☐ Male ☐ Female

8. Ethnicity ☐ Not Hispanic or Latino ☐ Hispanic or Latino (Complete Item 9)

9. Country/Area of Origin or Ancestry

10. Race *(Check all that apply)*
☐ White ☐ Asian
☐ Black or African American ☐ Native Hawaiian or Other Pacific Islander*
☐ American Indian/Alaska Native
Print Name of Enrolled/Principal Tribe _____ *complete Item 9

11. Is patient applying for ESRD Medicare coverage?
☐ Yes ☐ No

12. Current Medical Coverage *(Check all that apply)*
☐ Medicaid ☐ Medicare ☐ Employer Group Health Insurance
☐ DVA ☐ Medicare Advantage ☐ Other ☐ None

13. Height INCHES _____ OR CENTIMETERS _____

14. Dry Weight POUNDS _____ OR KILOGRAMS _____

15. Primary Cause of Renal Failure *(Use code from back of form)*

16. Employment Status *(6 mos prior and current status)*

Prior	Current	
☐	☐	Unemployed
☐	☐	Employed Full Time
☐	☐	Employed Part Time
☐	☐	Homemaker
☐	☐	Retired due to Age/Preference
☐	☐	Retired (Disability)
☐	☐	Medical Leave of Absence
☐	☐	Student

17. Co-Morbid Conditions *(Check all that apply currently and/or during last 10 years)* *See instructions

a. ☐ Congestive heart failure
b. ☐ Atherosclerotic heart disease ASHD
c. ☐ Other cardiac disease
d. ☐ Cerebrovascular disease, CVA, TIA*
e. ☐ Peripheral vascular disease*
f. ☐ History of hypertension
g. ☐ Amputation
h. Diabetes, currently on insulin
i. ☐ Diabetes, on oral medications
j. ☐ Diabetes, without medications
k. ☐ Diabetic retinopathy
l. ☐ Chronic obstructive pulmonary disease
m. ☐ Tobacco use (current smoker)
n. ☐ Malignant neoplasm, Cancer
o. ☐ Toxic nephropathy
p. ☐ Alcohol dependence
q. ☐ Drug dependence*
r. ☐ Inability to ambulate
s. ☐ Inability to transfer
t. ☐ Needs assistance with daily activities
u. ☐ Institutionalized
☐ 1. Assisted Living
☐ 2. Nursing Home
☐ 3. Other Institution
v. ☐ Non-renal congenital abnormality
w. ☐ None

18. Prior to ESRD therapy:

a. Did patient receive exogenous erythropoetin or equivalent?	☐ Yes	☐ No	☐ Unknown	If Yes, answer:	☐ 6-12 months	☐ >12 months
b. Was patient under care of a nephrologist?	☐ Yes	☐ No	☐ Unknown	If Yes, answer:	☐ 6-12 months	☐ >12 months
c. Was patient under care of kidney dietitian?	☐ Yes	☐ No	☐ Unknown	If Yes, answer:	☐ 6-12 months	☐ >12 months
d. What access was used on first outpatient dialysis:	☐ AVF	☐ Graft	☐ Catheter	☐ Other		
If not AVF, then: Is maturing AVF present?	☐ Yes	☐ No				
Is maturing graft present?	☐ Yes	☐ No				

19. Laboratory Values Within **45** Days Prior to the Most Recent ESRD Episode. (Lipid Profile within 1 Year of Most Recent ESRD Episode).

LABORATORY TEST	VALUE	DATE	LABORATORY TEST	VALUE	DATE
a.1. Serum Albumin (g/dl)	___ . ___		d. HbA1c	___ ___ . ___%	
a.2. Serum Albumin Lower Limit	___ . ___		e. Lipid Profile TC	___ ___ ___	
a.3. Lab Method Used (BCG or BCP)			LDL	___ ___ ___	
b. Serum Creatinine (mg/dl)	___ ___ . ___		HDL	___ ___	
c. Hemoglobin (g/dl)	___ ___ . ___		TG	___ ___ ___ ___	

B. COMPLETE FOR ALL ESRD PATIENTS IN DIALYSIS TREATMENT

20. Name of Dialysis Facility

21. Medicare Provider Number *(for item 20)*

22. Primary Dialysis Setting
☐ Home ☐ Dialysis Facility/Center ☐ SNF/Long Term Care Facility

23. Primary Type of Dialysis
☐ Hemodialysis (Sessions per week____/hours per session____)
☐ CAPD ☐ CCPD ☐ Other

24. Date Regular Chronic Dialysis Began ____/____/____ MM DD YYYY

25. Date Patient Started Chronic Dialysis at Current Facility ____/____/____ MM DD YYYY

26. Has patient been informed of kidney transplant options?
☐ Yes ☐ No

27. If patient NOT informed of transplant options, please check all that apply:
☐ Medically unfit ☐ Patient declines information
☐ Unsuitable due to age ☐ Patient has not been assessed
☐ Psychologically unfit ☐ Other

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C. COMPLETE FOR ALL KIDNEY TRANSPLANT PATIENTS

28. Date of Transplant ___/___/____ MM DD YYYY	29. Name of Transplant Hospital	30. Medicare Provider Number for Item 29

Date patient was admitted as an inpatient to a hospital in preparation for, or anticipation of, a kidney transplant prior to the date of actual transplantation.

31. Enter Date ___/___/____ MM DD YYYY	32. Name of Preparation Hospital	33. Medicare Provider number for Item 32

34. Current Status of Transplant *(if functioning, skip items 36 and 37)* ☐ Functioning ☐ Non-Functioning	35. Type of Donor: ☐ Deceased ☐ Living Related ☐ Living Unrelated
36. If Non-Functioning, Date of Return to Regular Dialysis ___/___/____ MM DD YYYY	37. Current Dialysis Treatment Site ☐ Home ☐ Dialysis Facility/Center ☐ SNF/Long Term Care Facility

D. COMPLETE FOR ALL ESRD SELF-DIALYSIS TRAINING PATIENTS (MEDICARE APPLICANTS ONLY)

38. Name of Training Provider	39. Medicare Provider Number of Training Provider (for Item 38)
40. Date Training Began ___/___/____ MM DD YYYY	41. Type of Training ☐ Hemodialysis a. ☐ Home b. ☐ In Center ☐ CAPD ☐ CCPD ☐ Other
42. This Patient is Expected to Complete *(or has completed)* Training and will Self-dialyze on a Regular Basis. ☐ Yes ☐ No	43. Date When Patient Completed, or is Expected to Complete, Training ___/___/____ MM DD YYYY

I certify that the above self-dialysis training information is correct and is based on consideration of all pertinent medical, psychological, and sociological factors as reflected in records kept by this training facility.

44. Printed Name and Signature of Physician personally familiar with the patient's training a.) Printed Name b.) Signature c.) Date ___/___/____ MM DD YYYY	45. UPIN of Physician in Item 44

E. PHYSICIAN IDENTIFICATION

46. Attending Physician *(Print)*	47. Physician's Phone No. ( )	48. UPIN of Physician in Item 46

PHYSICIAN ATTESTATION

I certify, under penalty of perjury, that the information on this form is correct to the best of my knowledge and belief. Based on diagnostic tests and laboratory findings, I further certify that this patient has reached the stage of renal impairment that appears irreversible and permanent and requires a regular course of dialysis or kidney transplant to maintain life. I understand that this information is intended for use in establishing the patient's entitlement to Medicare benefits and that any falsification, misrepresentation, or concealment of essential information may subject me to fine, imprisonment, civil penalty, or other civil sanctions under applicable Federal laws.

49. Attending Physician's Signature of Attestation *(Same as Item 46)*	50. Date ___/___/____ MM DD YYYY
51. Physician Recertification Signature	52. Date ___/___/____ MM DD YYYY

53. Remarks

F. OBTAIN SIGNATURE FROM PATIENT

I hereby authorize any physician, hospital, agency, or other organization to disclose any medical records or other information about my medical condition to the Department of Health and Human Services for purposes of reviewing my application for Medicare entitlement under the Social Security Act and/or for scientific research.

54. Signature of Patient *(Signature by mark must be witnessed.)*	55. Date ___/___/____ MM DD YYYY

G. PRIVACY STATEMENT

The collection of this information is authorized by Section 226A of the Social Security Act. The information provided will be used to determine if an individual is entitled to Medicare under the End Stage Renal Disease provisions of the law. The information will be maintained in system No. 09-70-0520, "End Stage Renal Disease Program Management and Medical Information System (ESRD PMMIS)", published in the Federal Register, Vol. 67, No. 116, June 17, 2002, pages 41244-41250 or as updated and republished. Collection of your Social Security number is authorized by Executive Order 9397. Furnishing the information on this form is voluntary, but failure to do so may result in denial of Medicare benefits. Information from the ESRD PMMIS may be given to a congressional office in response to an inquiry from the congressional office made at the request of the individual; an individual or organization for research, demonstration, evaluation, or epidemiologic project related to the prevention of disease or disability, or the restoration or maintenance of health. Additional disclosures may be found in the *Federal Register* notice cited above. You should be aware that P.L.100-503, the Computer Matching and Privacy Protection Act of 1988, permits the government to verify information by way of computer matches.

Appendix B. Diagnosis, Procedure, and Event Codes

Comorbidity	**ICD-9-CM Diagnosis codes**
ASHD	410.x-414.x, V45.81, V45.82
CHF	398.91, 422.x, 425.x, 428.x, 402.x1, 404.x1, 404.x3, V42.1
CVA	430.x-438.x
PVD	440.x-444.x, 447.x, 451.x-453.x, 557.x
Other Cardiac	420.x, 421.x, 423.x, 424.x, 429.x, 785.0-785.3, V42.2, V43.3
COPD	491.x-494.x, 496.x, 510.x
GI Disease	456.0-456.2, 530.7, 531.x-534.x, 569.84, 569.85, 578.x
Liver Disease	570.x, 571.x, 572.x, 572.4, 573.1-573.3, V42.7
Dysrhythmia	426.x, 427.x, V45.0, V53.3
Cancer	140.x-172.x, 174.x-208.x, 230.x, 231.x, 233.x, 234.x
Diabetes	250.x, 357.2, 362.0, 366.41
Anemia	280.x-285.x
CKD	016.0, 095.4, 189.0, 189.9, 223.0, 236.91, 250.4, 271.4, 274.1, 283.11, 403.x1, 404.x2, 404.x3, 440.1, 442.1, 447.3, 572.4, 580.x-588.x, 591.x, 642.1, 646.2, 753.12-753.17, 753.19, 753.2, 794.4
Hypertension	362.11, 401.x-405.x, 437.2

Event	**ICD-9-CM Codes/CPT Codes**
AVF insertion	36818, 36819, 36820, 36821, 36825 (CPT)
Infection	001.x-139.x, 254.1, 320.x-326.x, 331.81, 372.0-372.29, 373.0-373.2, 382.0-382.4, 383.0, 386.33, 386.35, 388.60, 390.x-393.x, 421.0, 421.1, 422.0, 422.91-422.93, 460.x-466.x, 472.x-474.0, 475.x, 476.1, 478.21-478.24, 478.29, 480.x-490.x, 491.1, 494.x, 510.x, 511.x, 513.0, 518.6, 519.01, 522.5, 522.7, 527.3, 528.3, 540.x-542.x, 566.x, 567.x, 569.5, 572.0, 572.1, 573.1-573.3, 575.0-575.12, 590.x, 595.0-595.4, 597.0-597.89, 598.x, 599.0, 601.x, 604.x, 607.1, 607.2, 608.0, 608.4, 611.0, 614.x-616.1, 616.3, 616.4, 616.8, 670.x, 680.x-686.x, 706.0, 711.x, 730.0-730.3, 730.8, 730.9, 790.7, 790.8, 996.60-996.69, 997.62, 998.5, 999.3
VA Infection	996.62 (ICD-9-CM diagnosis)
VA Complication	996.1, 996.73 (ICD-9-CM diagnosis)

Appendix C. The Selection-Corrected Cost Model

We start by assuming that selection into one of the three treatment groups ($z_i = 1, 2, or\ 3$), is determined by an unobserved latent variable, $z_i^* = \alpha' w_i + u_i$ where $u_i \sim N(0,1)$ and w_i is a vector of observable characteristics. Then,

$$z_i = \begin{cases} 1\ if\ -\infty < z_i^* \leq c_1 \\ 2\ if\ c_1 < z_i^* \leq c_2 \\ 3\ if\ c_2 < z_i^* < \infty \end{cases}$$

where c_1 and c_2 are unknown. This is the usual ordered probit model, and can clearly be re-written as:

$$z_i = \begin{cases} 1\ if\ u_i \leq c_1 - \alpha' w_i \\ 2\ if\ c_1 - \alpha' w_i < u_i \leq c_2 - \alpha' w_i \\ 3\ if\ c_2 - \alpha' w_i < u_i \end{cases}$$

Incidentally, we can see from this that the probability of selection into each group is as follows:

$$P(z_i = 1) = \Phi(c_1 - \alpha' w_i)$$
$$P(z_i = 2) = \Phi(c_2 - \alpha' w_i) - \Phi(c_1 - \alpha' w_i)$$
$$P(z_i = 3) = 1 - \Phi(c_2 - \alpha' w_i)$$

Then, if y_{ij} represents log(cost) for each person *i* in treatment group *j*, the cost model for each treatment group has the form:

$$y_{ij} = \beta_j' x_i + \varepsilon_{ij} \quad if\ \ z_i = j$$

where $\varepsilon_{ij} \sim N(0, \sigma_j^2)$. In this form, the selection problem is due to the fact that we believe ε_{ij} and u_i are correlated. If we assume that they are bivariate normal with correlation ρ_j, we can derive an expression for the conditional expectation $E[\varepsilon_{ij} | z_i = j]$. Specifically, it can be shown that:

$$E\left[\varepsilon_{ij} \middle| z_i = j\right] = \int_{c_{j-1} - \alpha' w_i}^{c_j - \alpha' w_i} f(\varepsilon_j | u_i) \cdot f(u_i) du_i$$
$$= \rho_j \sigma_j \frac{\phi(c_{j-1} - \alpha' w_i) - \phi(c_j - \alpha' w_i)}{\Phi(c_j - \alpha' w_i) - \Phi(c_{j-1} - \alpha' w_i)}$$
$$= \rho_j \sigma_j \lambda_i$$

Thus, we have

$$E\left[y_{ij} \middle| z_i = j\right] = \beta_j' x_i + E[\varepsilon_{ij} | z_i = j]$$
$$= \beta_j' x_i + \rho_j \sigma_j \lambda_i$$

Note that λ_i can be simplified for the first and third treatment groups:

$$\lambda_i = \begin{cases} \dfrac{-\phi(c_1 - \alpha' w_i)}{\Phi(c_1 - \alpha' w_i)} & if\ z_i = 1 \\ \dfrac{\phi(c_1 - \alpha' w_i) - \phi(c_2 - \alpha' w_i)}{\Phi(c_2 - \alpha' w_i) - \Phi(c_1 - \alpha' w_i)} & if\ z_i = 2 \\ \dfrac{\phi(c_2 - \alpha' w_i)}{1 - \Phi(c_2 - \alpha' w_i)} & if\ z_i = 3 \end{cases}$$

Estimating the selection-corrected cost model can be done either through full-information maximum likelihood, estimating all parameters at once, or it can be done in a two-step process that is slightly more robust to the normality assumption.

In the two-step process, the ordered probit model is fit to estimate α as well as c_1 and c_2. Those estimates are then used to estimate λ_i for each person, call it $\widehat{\lambda_i}$. Then, the cost model for each treatment group is estimated with $\widehat{\lambda_i}$ included as another regressor, with θ_j representing its coefficient. So, for each treatment group, *j*, the cost model becomes:

$$y_{ij} = \beta_j' x_i + \theta_j \widehat{\lambda_i} + \varepsilon_{ij}$$

Clearly θ_j is actually $\rho_j \sigma_j$, and when we obtain maximum likelihood estimates of θ_j and σ_j, we can easily compute ρ_j.

As was stated in the Methodology Section, identification is strengthened if we include an instrumental variable in w_i that is not in x_i.

Further details of how this model is estimated and used for predictions are available in Chiburis (2007).

Appendix D. The Endogenous-Switching Poisson Model

Following what is presented in Miranda (2004), we assume that the response variable, y_i, which in our case is the number of hospitalizations for a particular event, follows a Poisson Distribution:

$$f(y_i) = \frac{\exp\left[-\exp\left(x_i'\beta + \gamma d_i + \varepsilon_i\right)\right]\left[\exp\left(x_i'\beta + \gamma d_i + \varepsilon_i\right)\right]^{y_i}}{y_i!}$$

where x_i is a vector of variables and d_i is a dichotomous variable representing an endogenous switching (or selection) variable. In our case d_i indicates the presence of a mature AVF at dialysis initiation. We assume that the observed value of d_i is determined by a latent process described as follows:

$$d_i = \begin{cases} 1 & \text{if } z_i'\alpha + \upsilon_i > 0 \\ 0 & \text{otherwise} \end{cases}$$

where z_i is a vector of variables. We also assume that ε_i and υ_i are jointly normal with mean zero and covariance matrix:

$$\Sigma = \begin{pmatrix} \sigma^2 & \sigma\rho \\ \sigma\rho & 1 \end{pmatrix}$$

We can write the joint distribution of y_i and d_i as:

$$f(y_i, d_i|w_i) = \frac{1}{\sqrt{\pi}} \int [d_i \cdot f(y_i|d_i = 1, \varepsilon_i) P(d_i = 1|\varepsilon_i) + (1 - d_i) f(y_i|d_i = 0, \varepsilon_i) P(d_i = 0|\varepsilon_i)] f(\varepsilon_i) d\varepsilon_i$$

And if we let w_i represent all exogenous variables and define a new variable as follows:

$$\eta_i = \frac{\varepsilon_i}{\sigma\sqrt{2}}$$

then we can eventually produce the joint conditional distribution of y_i and d_i as:

$$f(y_i, d_i|w_i) = \frac{1}{\sqrt{\pi}} \int \left[f\left(y_i \middle| d_i, w_i, \sigma\eta_i\sqrt{2}\right)\left[d_i \Phi^*\left(\sigma\eta_i\sqrt{2}\right) + (1 - d_i)\Phi^*(-\sigma\eta_i\sqrt{2}\right]\right] exp(-\eta_i^2) d\eta_i$$

where

$$\Phi^*\left(\sigma\eta_i\sqrt{2}\right) = \Phi\left(\frac{z_i'\alpha + \rho\eta_i\sqrt{2}}{\sqrt{1 - \rho^2}}\right)$$

The form of the log likelihood is relatively simple:

$$L = \sum_{i=1}^{n} \ln[f(y_i, d_i|w_i)]$$

The change in variable facilitates Gauss-Hermite quadrature to approximate the integral, so that standard maximum likelihood techniques can be used to estimate the parameters. Likelihood ratio tests can be used to test the significance of the estimates. Specifically, a test on ρ represents a test on the endogeneity of d_i, since if $\rho = 0$, ε_i and v_i are independent, and there is no significant endogeneity in the selection.

Appendix E. Table Abbreviations

ASHD	Atherosclerotic Heart Disease
CHF	Congestive Heart Failure
CVA	Cerebrovascular Attack (Stroke)
PVD	Peripheral Vascular Disease
COPD	Chronic Obstructive Pulmonary Disease
GI	Gastrointestinal Disease
CKD	Chronic Kidney Disease
HTN	Hypertension
DM	Diabetes Mellitus
Nephrology Days	Number of Days prior to Dialysis initiation when the first nephrologist claim occurred
Geographic deciles	County-level deciles based on Dartmouth Atlas average reimbursement per Medicare beneficiary