Manufacturing & Service Operations Management

Publication details, including instructions for authors and subscription information:
http://pubsonline.informs.org

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M&SOM MANUFACTURING & SERVICE OPERATIONS MANAGEMENT
Vol. 17, No. 4, Fall 2015, pp. 608–619
ISSN 1523-4614 (print) | ISSN 1526-5498 (online)

informs
http://dx.doi.org/10.1287/msom.2015.0552

Optimal Vascular Access Choice for Patients on Hemodialysis

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Which vascular access to use is considered one of the most important questions in the care of patients on hemodialysis (HD). An arteriovenous fistula (AVF) is often considered the gold standard for delivering HD due to better patient survival, higher quality of life, and fewer complications. However, AVFs have some limitations: they require surgery, it takes approximately three months to know whether the surgery was successful, and a majority of these surgeries end in failure. Conversely, another common vascular access, the central venous catheter, can be inserted via a simple procedure and used immediately after placement. In this research, we address the question of whether and when to perform AVF surgery on incident and established HD patients, with the aim of finding individualized policies that maximize a patient's probability of survival and remaining quality-adjusted life expectancy. Using a continuous-time dynamic programming model and under certain data-driven assumptions, we establish structural properties of the optimal policy for each objective. We provide further insights for policy makers through our numerical experiments.

Keywords: dynamic programming; medical decision making; optimal treatment policies; hemodialysis; vascular access
History: Received: August 22, 2014; accepted: May 18, 2015. Published online in *Articles in Advance* August 10, 2015.

1. Introduction

End-stage renal disease (ESRD), the final stage of chronic kidney disease (CKD), occurs when the kidneys can no longer perform their essential task of removing waste products from the blood. Patients with ESRD require one of two interventions to stay alive: dialysis or kidney transplantation. Dialysis refers to the removal of waste and excess water from the body by circulating blood through a filter surrounded by clean fluid. Although kidney transplantation yields better patient outcomes (Tonelli et al. 2011), the demand for organs far outstrips the available supply, and nearly 100,000 patients await a kidney transplant in the United States (United Network for Organ Sharing 2014). Therefore, dialysis is the only realistic treatment option for the majority of patients with ESRD.

Hemodialysis (HD) is the most common form of dialysis, accounting for 92% of the incident dialysis cases in 2011 (U.S. Renal Data System 2013). HD involves the circulation of blood from a patient through a dialysis machine. The blood stream is typically accessed in one of two ways: by creation of an arteriovenous fistula (AVF) or by insertion of a central venous catheter (CVC). An AVF is created by a surgical procedure in which an artery is connected to a vein in the lower or upper arm. By contrast, placing a CVC is a minor procedure in which synthetic tubing is inserted directly into a large vein, usually in the neck. The AVF is often considered the gold standard for vascular access (National Kidney Foundation 2006) because it is associated with lower infection and mortality rates (Perl et al. 2011) and higher quality of life (Gorodetskaya et al. 2005, Wasse et al. 2007). The preference for using AVFs for HD is underscored by the Fistula First Catheter Last (FFCL) coalition, whose mission is "to improve the survival and quality of life of hemodialysis patients by optimizing vascular access selection—which for most patients will be an AV fistula" (Fistula First Catheter Last 2015). Current guidelines reflect this by suggesting that patients on HD should be referred for an AVF surgery when possible (Jindal et al. 2006, National Kidney Foundation 2006).

Although the benefits of an AVF over a CVC may seem clear, there are some major differences between them that deserve careful consideration before recommending one access versus the other. First, a CVC can be used immediately after placement for HD, whereas an AVF requires a lead time of approximately three months from the time of surgical creation until it has matured for possible use in HD (Ethier et al. 2008). This is the time it takes for the vein used in the AVF to become thick and large enough to support the insertion of needles necessary for each HD session. However, a significant proportion of created AVFs (approximately 50%) do not mature to a point they can be used for HD (Lok 2007, Peterson et al. 2008). In these cases, patients and their doctors may decide to undergo a subsequent AVF surgery, provided there are still suitable vessels located elsewhere on the arms to allow for this (typically two locations on each arm may be considered). Furthermore, even if AVF creation is successful, a mature and functional AVF has a limited lifetime, with a 15% annual failure probability (Roy-Chaudhury et al. 2006, Radoui et al. 2011). Finally, although an AVF has quality-of-life and morbidity advantages relative to a CVC once it is in use for HD, it still has several disadvantages associated with it prior to that time. Because the procedure is more invasive than a CVC insertion, it brings about the usual concerns with any surgery (e.g., patient anxiety, infection, postoperative recovery). In some cases, an AVF creation might compromise the blood supply to the hand, which can lead to permanent tissue and neurological damage. Furthermore, AVFs impose physical limitations (e.g., heavy lifting with the AVF arm is not advised), and some patients find AVFs disfiguring. In summary, an AVF is superior to a CVC *conditional* on being available for *immediate use* in HD. However, that is not the decision faced by patients and their doctors. Instead, they must decide whether or not to begin the AVF creation process, with the uncertain outcomes, disutilities, and durations just described.

The renal community has recently begun debating the complexities of vascular access choice (O'Hare et al. 2010), raising concerns about whether "fistula first" should continue to be the treatment paradigm for all patients. Basile and Lomonte (2012) and Amerling (2012) discussed opposing views regarding whether or not AVF is the best vascular access for HD patients, and Lameire and Van Biesen (2012) commented on this debate. The decision is especially germane for the elderly population; Moist et al. (2012) suggested considering factors such as an elderly patient's remaining life expectancy and personal preferences when making a recommendation of vascular access. This relates to the growing momentum in the medical community to take a personalized and shared approach (between clinicians and patients) to medical decisions, rather than the one-size-fits-all approach of most clinical guidelines (Barry and Edgman-Levitan 2012). The need for individualized renal care has also been emphasized in Tamura et al. (2011).

The goal of our paper is to bring a data-driven, analytical approach to investigating if and when HD patients should undergo an AVF surgery. In the spirit of patient-centered care, we focus on the patient's perspective and consider objectives related to patient lifetime and quality-adjusted lifetime. Our study is also in line with the recent emphasis in the United States on the use of comparative effectiveness research (CER) for guiding evidence-based decision making in medicine (Sox and Greenfield 2009). The importance of CER for guiding renal disease treatments in particular is discussed in Boulware (2013). On a similar note, Moist et al. (2012) noted the importance of future quantitative studies evaluating the timing and type of vascular access to improve mortality and quality of life in elderly patients. Our work provides decision makers with both high-level analytical insights on AVF versus CVC decisions and quantitative studies to guide decisions specifically for different patient types (including the elderly).

The rest of our paper is outlined as follows. We begin with a literature review and outline our contributions in §2. Section 3 provides our modeling framework and assumptions. Section 4 contains our key analytical results. In §5, we apply our analytical model using data-driven parameters from the literature. Finally, we provide concluding remarks in §6.

2. Literature Review

In this section, we review existing literature related to our research in two categories: (1) operations research/management science (OR/MS) papers on the optimal timing of medical interventions and (2) clinical papers describing decision-analytic models of vascular access choice for renal disease patients.

2.1. Optimal Timing of Medical Interventions

Decisions regarding the optimal time to apply a medical treatment or screen patients for some disease have received growing attention in the OR/MS community in the past decade. For instance, Alagoz et al. (2004) developed a Markov decision model to investigate the optimal timing of a living-donor liver transplant to maximize a patient's quality-adjusted life expectancy (QALE). Shechter et al. (2008) addressed the question of when to initiate HIV treatment so as to maximize the expected lifetime or quality-adjusted lifetime of a patient. Maillart et al. (2008) and Ayer et al. (2012) applied partially observable Markov decision process models related to breast cancer treatment. Lee et al. (2008) used a simulation-based approximate dynamic programming algorithm to derive near-optimal strategies for initiation and management of dialysis therapy. Zhang et al. (2012) investigated the problem of optimal prostate biopsy referral decisions and proved the existence of a control-limit-type policy that maximizes a patient's QALE. Ayvaci et al. (2012) studied the effect of budgetary restrictions on breast cancer diagnostic decisions by solving a mixed-integer program that maximizes a patient's total QALE under resource constraints.

2.2. Vascular Access Choice

A number of decision-analytic models related to AVF decision making have appeared in the recent clinical literature. Xue et al. (2010) developed a Markov model to study the cost effectiveness of different vascular access alternatives among incident HD patients. They found that the decision of whether to use AVFs or arteriovenous grafts (AVGs), another type of vascular access used in HD, for patients with incident HD depends highly on the AVF maturation failure probability, and they suggested taking this into account for individualized access planning. Hiremath et al. (2011) compared two AVF creation timing policies for a 70-year-old patient with stage 4 CKD using a Markov model and reported life expectancy and quality-adjusted life expectancy as the outcomes. They recommended further research on patient preference and cost implications when making AVF creation recommendations. Using a data-driven Monte Carlo simulation model, Shechter et al. (2014) investigated policies of AVF surgery timing for CKD patients. They assessed two classes of AVF referral policies over a range of values in terms of patient expected lifetime, proportion of AVF incident HD patients, and proportion of unused AVFs. A recent study by Drew et al. (2015), using the framework of Xue et al. (2010), found that patient characteristics such as diabetes status and gender also affect the cost effectiveness of a vascular access choice.

2.3. Contributions

The purpose of this paper is to address the following questions: (1) whether new HD patients should undergo a surgery for AVF creation or not and (2) whether an AVF surgery should be performed on existing HD patients if a previous AVF fails. We aim to find individualized optimal policies that maximize a patient's probability of survival and remaining quality-adjusted life expectancy, and we consider how AVF timing policies depend on patient age.

Unlike existing papers on vascular access choice for HD patients, the recommendations of which are simulation based (Xue et al. 2010, Hiremath et al. 2011, Drew et al. 2015), our research tackles the problem analytically. For instance, we prove the form of optimal policy for both lifetime and QALE metrics. Also, our paper provides the optimal decision for vascular access choice for the whole duration of a patient's dependency on HD, whereas existing literature only focuses on the vascular access decision at the time of HD initiation.

Existing recommendations for vascular access choice for HD-dependent patients do not appear evidence based and are not patient specific. We construct an analytical, data-driven model that incorporates several key factors when making AVF surgery decisions. In particular, patient age, AVF success probabilities, hazard rate functions for patient survival on an AVF versus CVC, and patient quality-of-life measures are important drivers of our model-based recommendations.

One of the key model components in determining the optimal policy, the AVF creation disutility, may be difficult to estimate and varies from patient to patient. To circumvent this issue, we introduce a dual view of the optimal policy by using the notion of a critical disutility. We prove that at each decision point, the nephrologist needs to know only if a patient's AVF creation disutility is below or above a critical factor, rather than its exact value, to make the optimal decision. This involves engaging patients in the decision-making process, by assessing their individual tolerances for undergoing surgery.

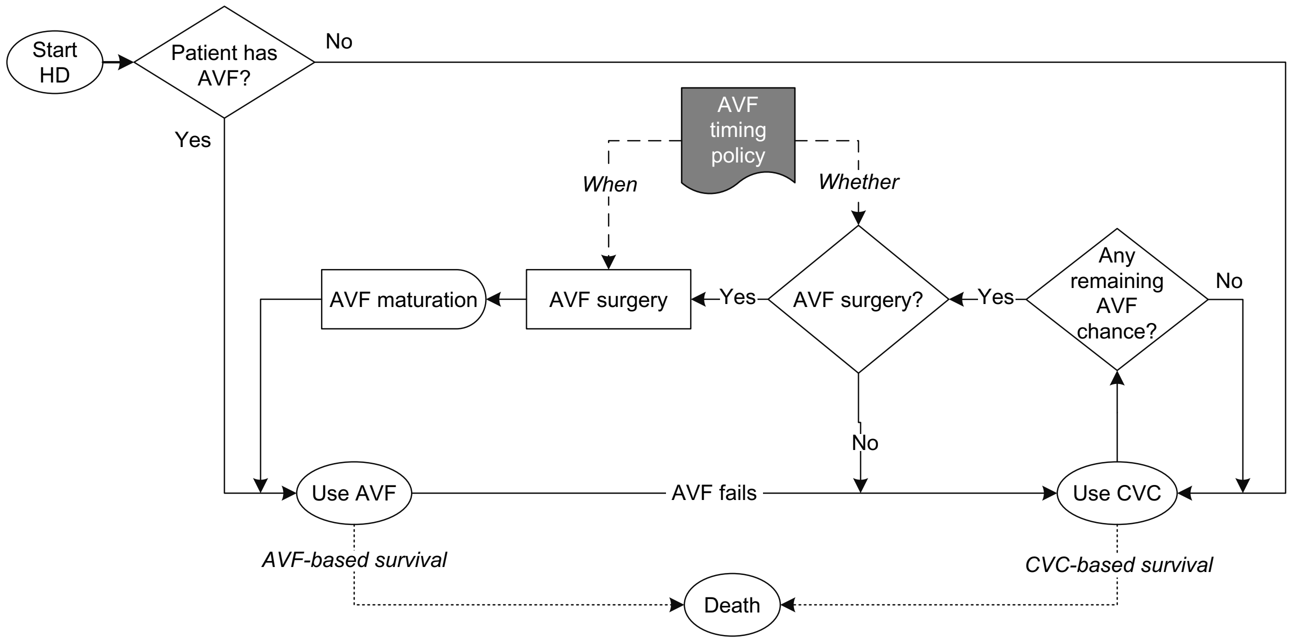
Several unique features of our research contribute to the OR/MS literature on medical decision making. We model a patient's lifetime as a continuous random variable, which facilitates our consideration of a patient's treatment-based nonstationary mortality rate. One key difference between our framework and other clinical decision-making papers in the literature is that we consider treatment options that require a stochastic lead time before they are effective. Whereas the previous models can assume that a mammography, transplantation, or HIV treatment can be administered whenever it is desired, an AVF cannot be created instantaneously. Moreover, there is uncertainty regarding whether and when a successful AVF will be attained. This brings an interesting dynamic to the decision, because the benefit of the AVF may not be as substantial at the time it is ready; moreover, the patient may die beforehand.

3. Modeling Framework

We consider an ESRD patient already on HD with at least one unused AVF opportunity. Note that our model will answer two types of AVF creation timing questions: (1) Should patients who just begin HD on a CVC undergo an AVF surgery (assuming no AVF is already in process)? And (2) should patients who have an AVF fail during the course of HD undergo an AVF surgery? We assume that the patient chooses between two vascular access types: CVC and AVF. We discuss the role of AVGs in §6. In Figure 1, the decision-making framework is illustrated. As the decision flowchart suggests, we make the following assumption.

Assumption 1 (Decision Points). *A patient can undergo an AVF surgery at any time, provided there are remaining AVF opportunities and an AVF is not under preparation or being used.*

Figure 1 Modeling Framework for Vascular Access Dynamics (Including Decisions and Events) for an HD-Dependent Patient



Although it might be optimal to create a new AVF when the one being used is approaching the end of its lifetime, this is not done in practice, and thus we do not consider it here.

The dynamics and principles of the model can be summarized as follows. A patient receives HD via an AVF as long as she has an established one. When there is no functional AVF (either when one fails or, at the beginning of HD, when the patient starts HD without a functional AVF), the patient dialyzes via a CVC as a bridge access. During this time, the policy determines *whether* and *when* to perform AVF surgery on the patient. If the policy recommends an AVF surgery, the patient goes through the AVF creation process and waits until possibly attaining a functional AVF. If all AVF opportunities have been used up, or the policy recommends no further AVF creation, the patient remains on HD with a CVC until death.

We discuss clinical factors impacting the decision of whether and when to use AVF opportunities in the following sections.

3.1. Access-Based Patient Survival

Patient survival on HD depends on the vascular access being used (Kurella et al. 2007, Perl et al. 2011). The left panel of Figure 2, adapted from Perl et al. (2011), shows that patients receiving HD via an AVF experience stochastically better survival rates than those who receive it via a CVC. Nevertheless, the survival benefit of AVF over CVC, measured by the failure-rate difference, diminishes as a patient continues using HD (see the right panel of Figure 2). In addition, a patient's failure rate on either access type increases as the HD duration increases.

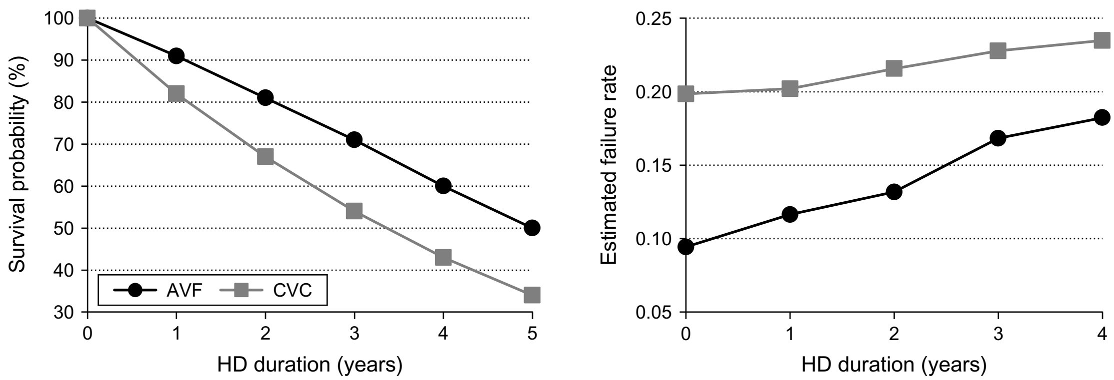
We use these data-driven observations to justify further assumptions below. First, we describe some notation:

- t: time since the patient started HD
- $\bar{\mathbf{F}}_X(t)$: survival probability function of a random variable X until time t ($\bar{\mathbf{F}}_X(t) = \mathbb{P}[X > t]$)
- $\mathbf{f}_X(t)$: probability density function of a random variable X at time t
- $\mathbf{r}_X(t)$: hazard rate function of a random variable X at time t
- X_t: residual lifetime of a random variable X at time t (a random variable denoting the remaining lifetime of X from time t onward, conditional on survival until time t)
- $\mu(t) \in \{a, c\}$: patient's HD access type at time t (a if it is an AVF and c if it is a CVC)
- C: random variable denoting patient's lifetime when remaining on a CVC from HD initiation time until death
- A: random variable denoting patient's lifetime when remaining on an AVF from HD initiation time until death
- L: random variable denoting patient's lifetime

Note that the distributions of C and A are dependent on a patient's age at the time HD commences, but we do not denote this dependency for ease of notation. Our next assumption describes how survival depends on HD duration and vascular access type.

Assumption 2 (Survival Distribution). *A patient's remaining survival only depends on the length of time that the patient has been on HD and the ongoing mode of HD access (an AVF or a CVC).*

Figure 2 **Access-Based Survival Probability and Failure Rate for a 67-Year-Old HD Patient**



Note. Access-based survival probability (left) is adapted from Perl et al. (2011), and failure rate (right) is estimated from survival probabilities.

Mathematically, Assumption 2 implies

$$\mathbb{P}(L_t \geq x \mid \mu(t') \text{ for all } t' \leq t, \mu(s) = a \text{ for all } t \leq s \leq x+t) = \bar{\mathbf{F}}_{A_t}(x), \tag{1}$$

$$\mathbb{P}(L_t \geq x \mid \mu(t') \text{ for all } t' \leq t, \mu(s) = c \text{ for all } t \leq s \leq x+t) = \bar{\mathbf{F}}_{C_t}(x). \tag{2}$$

We can explain Equation (1) (and similarly, Equation (2)) as follows. If a patient would remain on an AVF from t until $t+x$, her probability of surviving until $t+x$ is the same as a patient who has been on an AVF from the start of HD and has survived until t. Note that this assumption has been applied in related clinical research papers as well (see Xue et al. 2010, Drew et al. 2015, for instance).

The following are the definitions for common types of stochastic orders for random variables.

Definition 1 (Usual Stochastic Order). We say $X \leq_{st} Y$ if and only if $\bar{\mathbf{F}}_X(t) \leq \bar{\mathbf{F}}_Y(t)$: $\forall\, t$.

Definition 2 (Hazard Rate Order). We say $X \leq_{hr} Y$ if and only if $\mathbf{r}_Y(t) \leq \mathbf{r}_X(t)$: $\forall\, t$.

The following three assumptions formalize the data-driven observations of Figure 2, right panel.

Assumption 3 (Relative Performance). *The hazard rate of C is higher than or equal to the hazard rate of A at all ages. Mathematically, we have $\mathbf{r}_C(t) \geq \mathbf{r}_A(t)$ $\forall\, t$.*

Note that Assumption 3 corresponds to the CVC hazard rate curve lying above the AVF hazard rate curve in the right panel of Figure 2, and it is equivalent to $C \leq_{hr} A$ by definition. Throughout this paper, by *decreasing* (*increasing*), we mean “nonincreasing” (“nondecreasing”), unless “strictly” is noted.

Assumption 4 (Diminishing Difference). *The difference between hazard rates of C and A decreases in time; i.e., $\mathbf{r}_C(t) - \mathbf{r}_A(t)$ is decreasing in t.*

Note that Assumption 4 corresponds to the diminishing gap between the CVC hazard rate curve and the AVF hazard rate curve in the right panel of Figure 2. As we show in Lemma 3 of the online supplement (available at http://dx.doi.org/10.1287/msom.2015.0552), we have that $\mathbf{r}_C(t) - \mathbf{r}_A(t)$ is decreasing in t if and only if $\bar{\mathbf{F}}_C(t)/\bar{\mathbf{F}}_A(t)$ is log-convex in t.

Finally, the following assumption states that an HD patient’s mortality rate, on either access type, increases with patient age (or rather, we should more precisely say with “duration on HD”).

Assumption 5 (Diminishing Performance). *Random variables A and C have the increasing failure rate property; i.e., $\mathbf{r}_A(t)$ and $\mathbf{r}_C(t)$ are increasing in t.*

Assumption 5 is demonstrated by the fact that both curves in the right panel of Figure 2 are increasing.

We believe that assumptions posed on a patient’s survival (Assumptions 3–5) are intuitive. For instance, that a patient’s failure rates increase by age, or that the benefit of one intervention over another decreases with time, can be justified by the aging process and increasing presence of co-morbidities as a patient ages.

3.2. AVF Creation Process

After a patient and her clinician decide to use an AVF for HD, the patient visits a vascular surgeon for AVF placement. After the surgery is performed, the AVF maturation, a process by which a fistula becomes suitable to use for HD, begins (e.g., development of adequate flow, wall thickness, and diameter). It takes approximately three months of AVF maturation to learn whether the AVF is usable for HD. However, a major issue for AVF placement is that approximately 50% of AVFs fail to mature (Hakim and Himmelfarb 2009, Xue et al. 2010). Furthermore, even if an AVF creation is successful, it has an annual failure probability of 15% (Roy-Chaudhury et al. 2006, Radoui et al. 2011). These factors are critical to the decision of whether or not a patient should undergo an AVF surgery.

We use the following notation for random variables describing the AVF creation process:

- M_i: random variable denoting the maturation time of the ith AVF
- B_i: random variable denoting whether the creation of the ith AVF is successful ($B_i = 1$ if successful; 0 otherwise)
- Z_i: random variable denoting the total lifetime of the ith AVF given that it matures
- NF_t: number of failed AVFs creations up to time t

Note that NF_0 is not necessarily 0 because the patient may have AVF creations prior to HD initiation. We make the following assumption about the AVF creation process.

Assumption 6 (AVF Maturation and Lifetime). *All respective random variables describing the AVF creation process are stationary. Furthermore, M_i, and Z_i are identically distributed (across subsequent creations) and independent of the history of previous AVF creations.*

The stationarity of AVF creation variables is justified by the relatively short life expectancy of HD patients (average of 6.2 years; U.S. Renal Data System 2013). To the best of our knowledge, there is no evidence in the literature on the dependence of AVF maturation time and lifetime on the history of previous creations. However, it is natural to think that patients who fail to achieve a mature AVF on one attempt are more likely to have a failed creation in future attempts, and that the failure probability increases with the number of past AVF failures.

Assumption 7 (AVF Creation Success Probability). *The probability that an AVF matures is a decreasing function of NF, the number of previous maturation failures; i.e., $\mathbb{P}_t(B_i = 1 | NF_t)$ is decreasing in NF_t for any i.*

Henceforth, by *AVF surgery success*, we mean achieving a functional AVF after the maturation period.

3.3. Objective Functions

3.3.1. Total Lifetime. A natural metric for comparing policies is the total lifetime of a patient. Thus, we consider maximizing a patient's total lifetime (in the usual stochastic order) as one of the objective functions.

3.3.2. Quality-Adjusted Life Expectancy. Using AVF for HD not only brings better survival but also has a slightly higher quality of life for the patient, in comparison with HD using a CVC (Gorodetskaya et al. 2005, Wasse et al. 2007). Nevertheless, the process of AVF creation has some disutility associated with it, which can be attributed to the surgery and postsurgery inconveniences, complications, or costs. We define a patient's quality-adjusted life expectancy as the quality-adjusted lifetime on each vascular access minus the AVF surgery disutility for each AVF surgery performed (whether successful or not).

The following parameters are used in defining a patient's QALE:

- q_a, q_c: utility of being an HD patient who receives HD via an AVF or a CVC, respectively.
- d: AVF creation disutility

Based on the estimates in the literature (Gorodetskaya et al. 2005, Wasse et al. 2007), we make the following assumption about the access-based quality-of-life coefficients.

Assumption 8 (Relative Quality of Life). *Patients experience a better quality of life dialyzing via an AVF than via a CVC; i.e., we assume $q_a \geq q_c$.*

3.4. Dynamic Programming Formulation

To explain the dynamics of the model to optimize a patient's QALE and prove our analytical results, we formalize the decision-making process with a dynamic programming model. The model components are as follows:

- *States*: The set of vectors (NF, n, t) consisting of NF, the number of previous AVF maturation failures, n, the number of AVF chances left, and t, the time since the patient started HD, corresponds to a living state, and the absorbing state Δ corresponds to the death state. Sufficiency of (NF, n, t) to represent a living state is justified by our assumptions on patient survival (Assumption 2) and AVF variables (Assumption 6). The choice of these variables to represent a patient's state will become clear when we discuss state transitions.
- *Actions*: At each state $(NF, n \geq 1, t)$, one of two actions can be taken: either to perform an AVF surgery at time $t+y$ or to perform no more AVF surgeries on the patient. Note that the no-more-AVF action is the case of AVF surgery at $y = \infty$. Nevertheless, we keep it in the action space for clarity. When $n = 0$, the only option is to remain on CVC for the remainder of the patient's lifetime (the no-more-surgeries action). The choice of the next AVF surgery time to represent actions in the modeling framework is justified by Assumption 1 about decision times.
- *Transitions*: Based on Assumption 1, we only need to consider transitions between "decision states" (i.e., the subset of living states for which the patient does not have a functional or maturing AVF but has AVF opportunities remaining), the first transition to state $(NF, 0, t)$, and the transition to state Δ.

From decision state $(NF, n \geq 1, t)$ and planning for surgery at $t + y$, the patient may transition to one of three possible states. If the AVF matures and the patient survives until $t_1 = t + y + M + Z$, she transitions to $(NF, n-1, t_1)$. If the AVF creation fails but the patient survives until $t_2 = t + y + M$, she transitions to $(NF+1, n-1, t_2)$. Otherwise, the patient does not survive until the next decision state and transitions to Δ.

• *Immediate reward*: The immediate reward consists of a patient's QALE from time t until the next living state or death time. If the decision is to remain on CVC until death (either because the policy in use recommends this or because the patient uses up her AVF chances), the patient receives an immediate reward equal to her CVC utility-weighted remaining lifetime ($q_c \mathbb{E} C_t$). Otherwise, at state (NF, n, t) and when the surgery is planned at $t + y$, the patient's immediate reward includes her expected weighted lifetime from time t until t' (the next decision time) or death time (sometime between t and t'), and it may include an AVF creation disutility (if she survives until $t+y$). The value of t' depends on whether AVF matures or not as it was discussed in the previous section.

We discuss the value function and other components of our dynamic programming model as needed in the proofs in the online supplement.

4. Analytical Results

In this section, we present analytical results. All of the proofs for the analytical results are given in the online supplement.

4.1. Total Lifetime

Our main result concerning total lifetime is that to maximize an HD patient's survival probability until any time t' (and, as a result, to maximize expected lifetime), she should undergo an AVF surgery as soon as an opportunity becomes available. We prove this in a stochastic ordering sense: an identical patient who undergoes an AVF surgery earlier than another patient lives stochastically longer than that patient.

Theorem 1. *Under Assumptions 1–6, delaying AVF surgery stochastically decreases a patient's lifetime.*

Note that the stochastic ordering result means that the immediate-surgery policy maximizes the chance a patient may survive until a kidney transplant, through either a deceased or living kidney donor (see Theorem 6).

We have the following general result regarding the difference in mean residual lifetimes of variables A and C.

Theorem 2 (Mean Residual Lifetime Difference). *Let A and C be any arbitrary random variables satisfying Assumptions 3–5. We have $\mathbb{E}[A_t] - \mathbb{E}[C_t]$ is decreasing in t.*

We can explain Theorem 2 intuitively as follows. Assumptions 3 and 4 imply that the absolute difference of hazard rates of variables A and C is decreasing in time. Also, using the definition of hazard rate function, we have $\mathbf{r}_{X_t}(s) = \mathbf{r}_X(t+s)$ for any random variable X and $t, s \geq 0$. Therefore, the difference of hazard rates of random variables $A_{t'}$ and $C_{t'}$ at any arbitrary time is less than that of A_t and C_t for any $t' \geq t$.

4.2. QALE

In this section, we prove the optimality of a class of policies for the QALE metric that we refer to as HD duration threshold polices. Let τ denote a policy that at state $(NF, n \geq 1, t)$ recommends an AVF surgery *immediately*, if $t < \tau(NF)$, and recommends a CVC otherwise. Then, we have the following.

Theorem 3 (Optimality of Threshold Policies). *Under Assumptions 1–8, there exists a threshold policy τ^* that maximizes the QALE of the patient.*

Corollary 1. *The optimal HD duration threshold, τ^*, is decreasing in NF.*

Note that the optimal policy is independent of the number of remaining AVF chances. In the next proposition, we prove that the optimal threshold can be found using a binary search.

Proposition 1 (Binary Search). *An optimal threshold policy can be found using a binary search for τ^* over $[0, t_{\max}]$, where $t_{\max}$ is a reasonable upper bound for τ^*.*

We can set $t_{\max}$ equal to the time at which the patient reaches the age of 100 years because patients never undergo AVF surgeries after that age.

4.3. Critical Disutility

The result of Theorem 3 assumes one already has an estimate of the patient's disutility for an AVF creation. However, this may be difficult to estimate precisely in practice. Also, the optimal HD duration threshold needs to be calculated for different values of NF. To circumvent these challenges, we introduce a dual view of the HD duration threshold policy. We show that at any time, the decision of whether to do an AVF surgery is determined by comparing the patient's AVF creation disutility with a critical value. Thus, to make a decision, we only need to know whether the AVF creation disutility is above the critical value or not, rather than require a precise estimate of the AVF disutility itself.

Theorem 4 (Critical Disutility). *Under Assumptions 1–8, for any HD duration t, there exists a nonnegative critical AVF creation disutility, denoted by $d^{cr}(NF, t)$, such that the optimal decision at time t is to perform an AVF surgery immediately if the patient's AVF creation* *disutility is less than the critical disutility (i.e., if $d < d^{cr}(NF, t)$) and to use a CVC for the rest of patient's life otherwise.*

The critical disutility at t is defined as the residual QALE difference between immediate AVF surgery at t before subtracting the AVF creation disutility and staying on a CVC until death for a patient with only one AVF chance. In Theorem 5, we show that the critical disutility is proportional to the success probability of the current AVF creation. Therefore, one can calculate the critical disutility for different values of NF by calculating it for some baseline AVF creation success probability and then multiplying it by some factor (the ratio of the current AVF success probability given NF previous failures to the baseline value).

Theorem 5. *Under Assumptions 1–8, the critical disutility is proportional to the AVF creation success probability.*

Based on the following corollary, we can use the critical disutility function to find the critical HD duration for patients with different values of AVF creation disutility $d > 0$.

Corollary 2 (Relationship Between Critical Disutility and Critical Duration). *Suppose Assumptions 1–8. Then, $\tau^*(NF) = \inf(t: d^{cr}(NF, t) \leq d)$.*

Note that Theorem 4 provides an alternative way of comparing the optimal policy for individual patients as follows: if the critical disutility for one patient is always smaller than another, then the first patient has a smaller HD duration threshold, given that both patients have the same AVF creation disutility.

4.4. Kidney Transplant

In this section, we investigate an extension to the basic model by considering kidney transplant as a possible renal replacement therapy (RRT) for the patient. Since kidney transplant provides the best long-term health outcomes for the patient (Tonelli et al. 2011), we assume that a patient's residual QALE on transplant is higher than on HD and that the patient switches to kidney transplant as their RRT as soon as she is offered a favorable donated kidney. In other words, we assume that the decision of whether to accept a kidney donation is exogenous to our model.

Let Ψ be the (stochastic) time until a favorable kidney donation becomes available. We assume that once the patient receives the donated kidney, her future survival is independent of her HD history. Then, we can easily show that Theorem 1 holds under the extended model as follows.

Theorem 6. *Under Assumptions 1–6, delaying AVF surgery stochastically decreases a patient's lifetime, when the patient receives a donated kidney at time Ψ.*

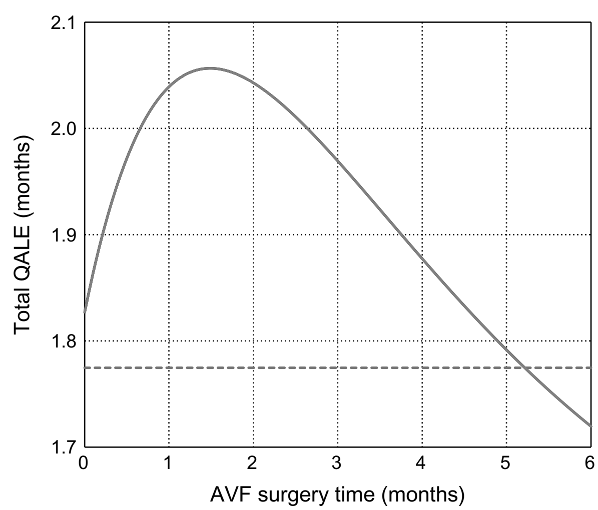
For the QALE metric on the other hand, the result of the basic model (optimality of threshold policies) does not necessarily extend even under a deterministic time until transplant. We show in the following example that the optimal policy can be neither immediate surgery nor staying on CVC forever (i.e., until transplant or death).

Consider a patient whose access-dependent lifetime on HD follows exponential distributions with means 3 and 1.5 months for AVF and CVC access types, respectively. Assume that the patient has a living donor who can donate a kidney after six months (the wait time can be due to medical tests the donor and patient should undergo, the operating room and surgeon availability, etc.). If the patient survives until transplant time, she receives 16 additional QALE months. Also assume that the maturation time is negligible, AVFs all mature and do not expire in the first six months, and $q_A = q_C = 1$.

In Figure 3, total QALE as a function of AVF surgery time for a patient with AVF disutility of three months is depicted. In this case, the optimal decision is to wait and perform surgery at $t = 1.5$ months. This demonstrates that the optimal policy is not of the form "perform AVF now or never."

We can explain the behavior observed in this example as follows. On the one hand, using the AVF for HD can benefit the patient by giving her a better quality of life as well as increasing her chances of survival until the transplant time. On the other hand, because of the AVF creation disutility, the AVF should not be used too early either because the patient may die well in advance of the transplant time. Therefore, the patient should use up some survival time without the AVF to increase the chance that when the AVF is

Figure 3 QALE Plot for a Patient with Transplant Option



Notes. The solid line depicts a patient's total QALE at $t = 0$ as a function of AVF surgery time. The dotted line shows total QALE when the patient stays on CVC until death or transplant.

Table 1 Baseline Parameters Used for Calculating the Critical Disutility

Variable	Value	Reference
On-HD survival (67-year-old)	—	Perl et al. (2011)
On-HD survival (82-year-old)	—	Kurella et al. (2007), Perl et al. (2011)
AVF primary failure probability (67-year-old)	50%	Lok (2007), Peterson et al. (2008)
AVF primary failure probability (82-year-old)	75%	Lok (2007), Peterson et al. (2008)
Yearly failure probability for a functional AVF	15%	Roy-Chaudhury et al. (2006), Radoui et al. (2011)
Maturation time (months)	Uniform(2, 4)	Lok (2007), Ethier et al. (2008)
Utility of dialysis with AVF	0.81	Gorodetskaya et al. (2005), Wasse et al. (2007)
Utility of dialysis with CVC	0.77	Gorodetskaya et al. (2005), Wasse et al. (2007)

created, it bridges the patient's survival until the time of transplant (and therefore the AVF creation is not wasted).

Although threshold policies may be suboptimal in general, we prove their optimality under additional assumptions in the following theorem. For this result, we assume the patient has a living donor and, thus, a deterministic time until transplant seems reasonable. Also, we assume that time until transplant is short enough that AVFs, if mature, do not expire before transplant time. Finally, we allow for the possibility of transplant cancellation, for instance, if the donor changes his mind or if the donated kidney is to be found incompatible as a result of the tests.

Theorem 7. *Suppose that the time until transplant, if it is not canceled, is deterministic, i.e., $\Psi = \psi$ for some known ψ, that $\bar{\mathbf{F}}_{A_t}(\psi - t) - \bar{\mathbf{F}}_{C_t}(\psi - t)$ is decreasing in t, and that an AVF's lifetime, if it matures, is greater than the time until transplant with probability* 1. *Then under Assumptions* 1–8, *there exists a threshold policy τ^* that maximizes the QALE of the patient.*

Note that $\bar{\mathbf{F}}_{A_t}(\psi - t)$ (and similarly, $\bar{\mathbf{F}}_{C_t}(\psi - t)$) can be interpreted as the survival probability of a patient on an AVF (CVC) until the transplant time, given her survival until t. The assumption that $\bar{\mathbf{F}}_{A_t}(\psi - t) - \bar{\mathbf{F}}_{C_t}(\psi - t)$ is decreasing in t is supported by the empirical data given in Perl et al. (2011). Also, Theorem 7 cannot be applied to the aforementioned example, because $\bar{\mathbf{F}}_{A_t}(\psi - t) - \bar{\mathbf{F}}_{C_t}(\psi - t)$ equals $e^{-(1/3)(6-t)} - e^{-(1/1.5)(6-t)}$, which is not a decreasing function.

5. Numerical Results

To demonstrate the results of Theorems 3 and 4, we performed a numerical study. The baseline values for different model parameters and sources used are given in Table 1.

For patients' HD survival, we used Perl et al. (2011), which provides only the first five years of survival outcomes for a cohort of 67-year-old patients. To obtain complete survival curves, we extrapolate the hazard rate functions so that Assumptions 3–5 are satisfied. Specifically, we assume that the AVF and CVC hazard rates increase linearly after the last observed hazard rate with slopes α_A and α_C, respectively. We need to assume $\alpha_A \geq \alpha_C \geq 0$, so that Assumptions 4 and 5 are satisfied. To have Assumption 3 met, we modify the hazard rates for CVC such that after the point the hazard rate curves meet (if they ever meet, which is always the case when $\alpha_A > \alpha_C$), we have that $\mathbf{r}_C(t) = \mathbf{r}_A(t)$, with the slope of the line equal to α_A (see Figure 4 for an illustration). We calculated the average rate of increase for the AVF and CVC hazard rate functions (that is the slope connecting the first and last observed hazard rates). Denoting these slopes with $\bar{\mathbf{r}}_A$ and $\bar{\mathbf{r}}_C$, respectively, we assumed $\alpha_A = \bar{\mathbf{r}}_A$ and $\alpha_C = \bar{\mathbf{r}}_C$ (below, we perform one-way sensitivity analyses by considering scenarios in which $\alpha_A = (1 \pm 25\%)\bar{\mathbf{r}}_A$ and $\alpha_C = (1 \pm 25\%)\bar{\mathbf{r}}_C$).

Based on the hazard rate functions, a 67-year-old patient's entire survival curve was calculated. We used the result of Theorem 4 to calculate the critical disutility as a function of HD duration using Monte Carlo simulation (see the proof of Theorem 4 in the online supplement). The left panel of Figure 5 shows the critical disutility under the baseline assumption for survival extrapolation. For example, a 67-year-old patient who has been on HD for two (three) years should undergo AVF surgery provided her AVF disutility is less than 85 (65) QALE days.

Figure 4 Base Case Hazard Rate Functions for a 67-Year-Old Patient's Lifetime On HD

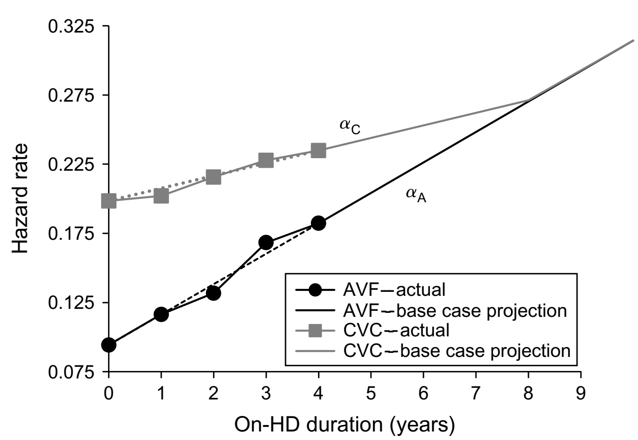
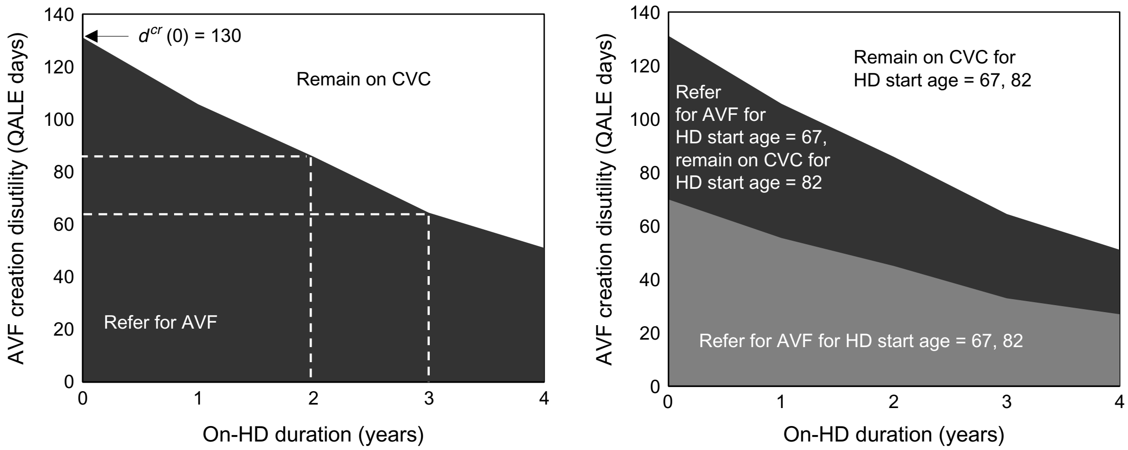


Figure 5 Critical Disutility and HD Duration for 67- and 82-Year-Old Patients



Notes. On the left, the critical HD duration for 67-year-old patients with AVF creation disutility of 65 and 85 QALE days is illustrated. It also shows that the critical disutility for a 67-year-old who just begins HD is 130 QALE days. On the right, the critical disutility for 67- and 82-year-old patients is illustrated.

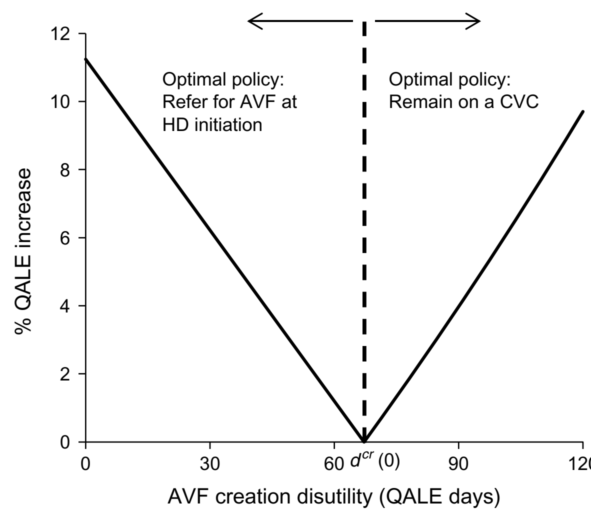
Note that we assume the same probability of AVF success, regardless of *NF*, because the clinical literature does not yet provide this detail when discussing maturation failure rates. Nevertheless, one can easily calculate the critical disutilities as a function of *NF* by multiplying the function by a proper factor (see Theorem 5 for more details).

Recall that the motivation for the critical disutility approach was for cases in which it might be difficult to estimate precisely a patient's disutility for the AVF surgery. However, based on Corollary 2, the left panel of Figure 5 can also be inverted to answer questions regarding a patient for whom a precise estimate of the AVF disutility is obtained. For example, the figure also indicates that if a 67-year-old patient has a disutility of 85 (65) QALE days, then she should undergo an AVF surgery as long has she has been on HD less than two (three) years.

To visualize the impact of age at HD initiation on the critical disutility, we have plotted the critical disutility curves for patients who start HD at ages of 67 and 82 years in Figure 5, right panel. As the plot shows, the critical disutility of the older patient is always smaller. For instance, for the time of HD initiation, a 67-year-old patient should undergo AVF surgery as long as her AVF creation disutility is below 130 QALE days, whereas for an 82-year-old patient, AVF surgery is advisable only when her AVF creation disutility is below 70 QALE days (Figure 5, right panel).

In Figure 6, we plot the percent QALE increase from the nonoptimal policy to the optimal policy as a function of the AVF creation disutility for an 82-year-old patient with one AVF chance, i.e., for $n = 1$. We have compared the two policies of "no AVF surgery" and "surgery at HD initiation," because they represent two opposing opinions in the literature (Basile and Lomonte 2012, Amerling 2012), and therefore the figure indicates what can be gained if a decision maker adheres to a suboptimal policy on one side of the threshold or the other. For $d < d^{cr}(0)$, the optimal policy is to perform AVF surgery on the patient at the time of HD initiation, whereas for $d \geq d^{cr}(0)$, the optimal policy is to remain on a CVC.

Figure 6 Percent Remaining QALE Increase from the Nonoptimal Policy to the Optimal Policy as a Function of the AVF Creation Disutility



Notes. We have compared the two policies of "no AVF surgery" and "surgery at HD initiation" for an 82-year-old patient with $n = 1$ (other parameters are given in Table 1), with the former being optimal for $d \geq d^{cr}(0)$ and the latter for $d \leq d^{cr}(0)$.

5.1. Sensitivity Analysis

We also performed a sensitivity analysis to see how robust the results are to the changes in the input parameters. The parameters and values tested for one-way and two-way sensitivity analyses and the corresponding critical disutilities at the time of HD

Table 2 Sensitivity Analysis for the Critical Disutility (QALE Days) of a 67-Year-Old HD Incident Patient Computed Using Monte Carlo Simulation

Parameter	Value	Critical disutility
N/A	Default	151
AVF surgery success probability	0.2	76
	0.6	223
Functional AVF annual failure rate	0.1	172
	0.2	134
Maturation time (months)	Uniform[3, 5]	150
	Uniform[4, 6]	149
	Uniform[1, 6]	150
QALE coeff. [CVC, AVF]	[0.73, 0.81]	164
	[0.75, 0.81]	158
	[0.81, 0.81]	139
Patient's survival projection parameters $[\alpha_A, \alpha_C]$	$[\bar{\mathbf{r}}_A, 1.25 * \bar{\mathbf{r}}_C]$	151
	$[\bar{\mathbf{r}}_A, 0.75 * \bar{\mathbf{r}}_C]$	150
	$[1.25 * \bar{\mathbf{r}}_A, \bar{\mathbf{r}}_C]$	147
	$[0.75 * \bar{\mathbf{r}}_A, \bar{\mathbf{r}}_C]$	155

Note. The default values for each parameter are given in Table 1.

initiation are given in Table 2. For instance, the critical disutilities for patients with 60% and 20% chances of success in having a matured AVF are 223 and 76 QALE days, respectively. Because the first patient has a higher chance of surgery success, she benefits from the surgery more than the other patient, and as a result, she should undergo AVF surgery at the time of HD initiation as long as her surgery disutility is less than 223 QALE days, whereas the other patient benefits from AVF surgery only when the surgery disutility is less than 76 QALE days. As the results in Table 2 suggest, the critical disutility is most sensitive to the AVF surgery success probability. Based on Theorem 5, the critical disutility is proportional to this parameter, and therefore, it can be easily adjusted by a nephrologist based on her perception of a patient's AVF surgery success probability or existing statistics in the local practice.

6. Conclusion

In this work, we considered the problem of vascular access choice between a CVC and an AVF for HD patients, with a goal of maximizing a patient's total lifetime and QALE. We analytically proved that delaying AVF surgery stochastically decreases a patient's lifetime. As a result, the policy of "use the next AVF (opportunity) as soon as a patient starts HD or when the one being used fails" maximizes a patient's survival probability. We also proved that the optimal policy to maximize a patient's QALE is of a threshold type: there is an HD duration threshold before which immediate surgery is the optimal choice, whereas after that time CVC is the optimal vascular access choice for the remainder of the patient's lifetime. This threshold depends on the number of past AVF maturation failures.

The AVF creation disutility plays an essential role in determining the critical HD duration of the QALE optimal policy. Because patients may feel differently about the disutility of AVF surgery, and also because it is not an easy parameter to elicit from a patient, our model provides an alternative way to make the optimal AVF timing decision. We showed that the decision of whether to perform an AVF surgery or not can be determined solely by comparing the patient's AVF creation disutility with a boundary value reflecting the prospective additional quality lifetime for the patient, which we refer to as the critical disutility. Thus, a nephrologist can inform the patient of the benefits and inconveniences of undergoing the AVF surgery, and then they can collectively decide whether to do the surgery. Even if a rough estimate of the patient's disutility for AVF surgery indicates that it is clearly below or above the critical disutility, it will be clear that the patient should or should not, respectively, undergo an AVF surgery. Estimates of a patient's disutilities can be obtained using standard elicitation methods in the medicaldecision-making community, such as the standard gamble, time trade-off, and visual analog scale (Gold et al. 1996). This also facilitates getting patients involved in the decision-making process, one of the key recommendations of the Institute of Medicine's report on patient-centered care, which has been emphasized in the medical community in the past decade (Institute of Medicine 2004).

We also found that the possibility of receiving a kidney transplant adds new complexities to the model and optimal policy structure. Although the optimal policy under the total lifetime remains the same, the result on QALE metric (optimality of threshold policies) does not necessarily extend, even when the time of transplant is known with certainty. Nevertheless, we provided a theorem proving that under additional assumptions (which are supported by data), threshold policies remain optimal.

The framework and analytical results of the paper may also be relevant to operational questions outside of healthcare, particularly in the area of machine maintenance and equipment reliability. For example, consider a machine with a vital component. If the component breaks down, it may be replaced with a cheap, available spare. Additionally, one may order a more expensive, higher-quality component, which involves a lead time for delivery. This is analogous to deciding whether and when to refer a patient for an AVF versus letting them continue to receive HD through a CVC. An AVF provides higher-quality HD outcomes compared to a CVC, but an AVF cannot be created quickly, and it is more expensive in the sense of the surgical disutility it imposes on patients.

Supplemental Material

Supplemental material to this paper is available at http://dx.doi.org/10.1287/msom.2015.0552.

Acknowledgments

M. R. Skandari is supported by the Natural Sciences and Engineering Research Council [Discovery Grant 341415-07]. S. Shechter is supported by the Career Investigator Award of the Michael Smith Foundation for Health Research. The authors thank the three referees, associate editor, and editor for their helpful comments and suggestions.

References

Alagoz O, Maillart LM, Schaefer AJ, Roberts MS (2004) The optimal timing of living-donor liver transplantation. *Management Sci.* 50(10):1420–1430.

Amerling R (2012) Con: On cardiovascular outcomes and the arteriovenous fistula: Lesser of evils. *Nephrology Dialysis Transplantation* 27(10):3756–3757.

Ayer T, Alagoz O, Stout NK (2012) A POMDP approach to personalize mammography screening decisions. *Oper. Res.* 60(5): 1019–1034.

Ayvaci MUS, Alagoz O, Burnside ES (2012) The effect of budgetary restrictions on breast cancer diagnostic decisions. *Manufacturing Service Oper. Management* 14(4):600–617.

Barry MJ, Edgman-Levitan S (2012) Shared decision making—The pinnacle of patient-centered care. *New England J. Medicine* 366(9):780–781.

Basile C, Lomonte C (2012) Pro: The arteriovenous fistula is a blessing of God. *Nephrology Dialysis Transplantation* 27(10): 3752–3756.

Boulware LE (2013) Comparative effectiveness research in kidney disease: A national priority. *Amer. J. Kidney Diseases* 61(1):9–12.

Drew D, Lok C, Cohen J, Wagner M, Tangri N, Weiner D (2015) Vascular access choice in incident hemodialysis patients: A decision analysis. *J. Amer. Soc. Nephrology* 26(1):183–191.

Ethier J, Mendelssohn DC, Elder SJ, Hasegawa T, Akizawa T, Akiba T, Canaud BJ, Pisoni RL (2008) Vascular access use and outcomes: An international perspective from the Dialysis Outcomes and Practice Patterns Study. *Nephrology Dialysis Transplantation* 23(10):3219–3226.

Fistula First Catheter Last (2015) Fistula First Catheter Last coalition. Accessed July 29, 2015, http://esrdncc.org/ffcl/about-us-fistula-first/.

Gold MR, Siegel JE, Russell LB, Weinstein MC (1996) *Cost-Effectiveness in Health and Medicine* (Oxford University Press, New York).

Gorodetskaya I, Zenios S, McCulloch CE, Bostrom A, Hsu C, Bindman AB, Go AS, Chertow GM (2005) Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney Internat.* 68(6):2801–2808.

Hakim RM, Himmelfarb J (2009) Hemodialysis access failure: A call to action revisited. *Kidney Internat.* 76(10):1040–1048.

Hiremath S, Knoll G, Weinstein MC (2011) Should the arteriovenous fistula be created before starting dialysis? A decision analytic approach. *PLoS ONE* 6(12):e28453.

Institute of Medicine (2004) Insuring America's health: Principles and recommendations. Report, National Academy of Sciences, Washington, DC. http://www.iom.edu/Reports/2004/Insuring-Americas-Health-Principles-and-Recommendations.aspx.

Jindal K, Chan CT, Deziel C, Hirsch D, Soroka SD, Tonelli M, Culleton BF (2006) Hemodialysis clinical practice guidelines for the Canadian Society of Nephrology. *J. Amer. Soc. Nephrology* 17(3, Suppl 1):S16–S23.

Kurella M, Covinsky KE, Collins AJ, Chertow GM (2007) Octogenarians and nonagenarians starting dialysis in the United States. *Ann. Internal Medicine* 146(3):177–183.

Lameire N, Van Biesen W (2012) A "secular" view on vascular access in haemodialysis. *Nephrology Dialysis Transplantation* 27(10):3758–3761.

Lee CP, Chertow GM, Zenios SA (2008) Optimal initiation and management of dialysis therapy. *Oper. Res.* 56(6):1428–1449.

Lok CE (2007) Fistula First Initiative: Advantages and pitfalls. *Clinical J. Amer. Soc. Nephrology* 2(5):1043–1053.

Maillart LM, Ivy JS, Ransom S, Diehl K (2008) Assessing dynamic breast cancer screening policies. *Oper. Res.* 56(6):1411–1427.

Moist LM, Lok CE, Vachharajani TJ, Xi W, AlJaishi A, Polkinghorne KR, Vazquez M, Lee TC (2012) Optimal hemodialysis vascular access in the elderly patient. *Semin. Dialysis* 25(6):640–648.

National Kidney Foundation (2006) KDOQI clinical practice guidelines for vascular access. *Amer. J. Kidney Diseases* 48(Suppl 1): S176–S247.

O'Hare A, Allon M, Kaufman JS (2010) Whether and when to refer patients for predialysis AV fistula creation: Complex decision making in the face of uncertainty. *Semin. Dialysis* 23(5):452–455.

Perl J, Wald R, McFarlane P, Bargman JM, Vonesh E, Na Y, Jassal SV, Moist L (2011) Hemodialysis vascular access modifies the association between dialysis modality and survival. *J. Amer. Soc. Nephrology* 22(6):1113–1121.

Peterson WJ, Barker J, Allon M (2008) Disparities in fistula maturation persist despite preoperative vascular mapping. *Clinical J. Amer. Soc. Nephrology* 3(2):437–441.

Radoui A, Lyoussfi Z, Haddiya I, Skalli Z, Idrissi RE, Rhou H, Ezzaitouni F, et al. (2011) Survival of the first arteriovenous fistula in 96 patients on chronic hemodialysis. *Ann. Vascular Surgery* 25(5):630–633.

Roy-Chaudhury P, Sukhatme VP, Cheung AK (2006) Hemodialysis vascular access dysfunction: A cellular and molecular viewpoint. *J. Amer. Soc. Nephrology* 17(4):1112–1127.

Shechter SM, R SM, Zalunardo N (2014) Timing of arteriovenous fistula creation in patients with CKD: A decision analysis. *Amer. J. Kidney Diseases* 63(1):95–103.

Shechter SM, Bailey MD, Schaefer AJ, Roberts MS (2008) The optimal time to initiate HIV therapy under ordered health states. *Oper. Res.* 56(1):20–33.

Sox HC, Greenfield S (2009) Comparative effectiveness research: A report from the Institute of Medicine. *Ann. Internal Medicine* 151(3):203–205.

Tamura MK, Tan JC, O'Hare AM (2011) Optimizing renal replacement therapy in older adults: A framework for making individualized decisions. *Kidney Internat.* 82(3):261–269.

Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, Klarenbach S, Gill J (2011) Systematic review: Kidney transplantation compared with dialysis in clinically relevant outcomes. *Amer. J. Transplantation* 11(10):2093–2109.

United Network for Organ Sharing (2014) United Network for Organ Sharing home page. Accessed February 1, 2014, http://www.unos.org/.

U.S. Renal Data System (2013) 2013 atlas of CKD and ESRD. Annual data report, U.S. Renal Data System, Ann Arbor, MI.

Wasse H, Kutner N, Zhang R, Huang Y (2007) Association of initial hemodialysis vascular access with patient-reported health status and quality of life. *Clinical J. Amer. Soc. Nephrology* 2(4): 708–714.

Xue H, Lacson E Jr, Wang W, Curhan GC, Brunelli SM (2010) Choice of vascular access among incident hemodialysis patients: A decision and cost-utility analysis. *Clinical J. Amer. Soc. Nephrology* 5(12):2289–2296.

Zhang J, Denton BT, Balasubramanian H, Shah ND, Inman BA (2012) Optimization of prostate biopsy referral decisions. *Manufacturing Service Oper. Management* 14(4):529–547.