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Personalized Chronic Disease Follow-Up Appointments: Risk-Stratified Care Through Big Data

Zlatana Nenova*
University of Denver, Daniels College of Business, Denver, Colorado 80208, USA, zlatana.nenova@du.edu

Jennifer Shang
University of Pittsburgh, Katz Graduate School of Business, Pittsburgh, Pennsylvania 15260, USA, shang@katz.pitt.edu

Managing patients with chronic conditions is challenging. It requires timely care adjustments based on the patient's health status. We leverage big data to optimize patient monitoring frequencies and improve treatment. Our research is motivated by the need to improve patient care at the Veterans Affairs (VA) hospitals. We propose an integrated model to better serve patients with chronic kidney disease (CKD). CKD is prevalent, complex, and costly. The demand for kidney care has steadily increased; however, there is a decline in the availability of nephrologists. We propose a finite-horizon Markov decision process (MDP) model, which utilizes evidence-based and data-driven approach to identify the best follow-up appointment schedule for patients. The MDP model helps attain an optimal dynamic treatment plan to enhance patient's quality of life. It is parameterized by data from 11 US Department of Veterans Affairs hospitals, containing 68,513 CKD patients (mostly males between 60 and 90 years old) geographically dispersed throughout the United States between January 1, 2009 and February 21, 2016. Through various estimates and assumptions, we propose an optimal monitoring policy. We find that CKD severity, comorbidities, age, and distance to nephrologist all play roles in shaping patients' needs of care. Through the VA clinical data, we have numerically validated our recommendation and shown that it considerably outperforms the current kidney care guidelines adopted by the VA.

Key words: chronic disease management; Markov decision process; chronic disease monitoring
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*Corresponding author.

> *Kidney disease doesn't get the attention, funding or concern associated with cancers of the breast or prostate. But it actually kills more Americans – 90,000 a year – than both malignancies combined.*
>
> Brody 2013

1. Introduction

Chronic kidney disease (CKD) is characterized by a decline in the filtration functions of patient's kidneys. The laboratory value used to estimate kidney functionality is called glomerular filtration rate (GFR). Due to high laboratory cost, GFR is estimated (eGFR) using age, race, gender, and blood creatinine information (Levey et al. 2006). eGFR results are used to classify patients into five different CKD stages. Patients are assigned to CKD Stage 1 or 2 if their eGFR ≥ 60, CKD Stage 3 if their eGFR $\in [30,60)$, Stage 4 if eGFR $\in [15,30)$, and Stage 5 if eGFR $\in (0,15)$. The most advanced state of the 5th stage is called end-stage renal disease (ESRD). ESRD is reached when a patient experiences a complete kidney failure, and needs dialysis or a kidney transplant.

1.1. The Need for Better CKD Monitoring and Treatment

Chronic kidney disease is the ninth leading cause of death in the United States (NCHS/National Center for Health Statistics 2016). It is estimated that between 11% and 16.8% of the US population has CKD (Centers for Disease Control and Prevention 2007, Coresh et al. 2003). It is largely asymptomatic in its early stages (stages 1 and 2), which could explain why only about 10% of all CKD patients are diagnosed (NIH/National Institutes of Health 2012). NKF/National Kidney Foundation (2017) notes that over 660,000 Americans are currently treated for kidney failure. Saran et al. (2016) report that every year there are approximately 21,000 new patients diagnosed with ESRD, and approximately 20% of all Medicare spending is for CKD patients. CKD is expensive to treat, as it is a disease multiplier—approximately 55% of all CKD patients have diabetes and self-reported cardiovascular disease (CVD) (NIH/National Institutes of Health 2012). These complexities could explain the high hospitalization rates and 30-day readmission rates, which pose a heavy financial burden on the healthcare system.

Like other chronic diseases, CKD cannot be reversed (Eddy 2005). Still, its progression can be slowed and even halted if proper care is administered (Drawz and Rosenberg 2013). Unfortunately, many studies found that kidney disease management has been suboptimal (Anavekar et al. 2004, Coresh et al. 2001, Hsu et al. 2001, Israni et al. 2003, Parikh et al. 2006, Patwardhan et al. 2007, Sharif et al. 2016, Tiwari et al. 2007). Standard CKD care involves nephrologist appointments, where patient's kidney function and comorbidities development are assessed, and a treatment plan for slowing kidney failure is chosen. To prevent further physical deterioration, CKD patients need to attend well-timed appointments. Visits should be scheduled so they are neither too frequent (thus overwhelming to the patient and the healthcare system) nor too scarce (thus insufficient in detecting progression early enough to prevent hospitalization and early death).

Current guidelines from the National Institute for Health and Care Excellence (NICE) in the United Kingdom suggest that patients in stages 1 and 2 should be seen once per year; every six months in stage 3; every three months in stage 4; and every one and half months in stage 5 (Mandal 2015, NICE/National Institute for Health and Care Excellence 2014, Stevens and Levin 2013). For similar recommendations given in the United States, see Levey et al. (2003), VA/Department of Veterans Affairs (2008), Inker et al. (2014). Like most population-based (i.e., not personalized) policies, NICE provides general guidance and is often suboptimal due to its inability to incorporate individual patient's demographic and comorbidity information. Furthermore, current guidelines do not consider disutilities associated with doctor visits that depend on one's mobility (Weiner and Seliger 2014). Mobility is particularly important for the patients in our study (US Veterans), as the American Community Survey by the U.S. Census Bureau finds that 24.1% of veterans live in rural areas. The median age of rural veterans is 15 years older than urban veterans, and this discrepancy increases with the level of rurality. Due to age, financial condition, and health complications, many rural veterans rely on a centralized transportation system (Veterans Transportation Program), which takes them to the regional medical center early in the morning and returns them late in the afternoon, regardless of their appointment time. This results in long waiting times, inconvenience, and extra hardship.

1.2. Chronic Disease Treatment Model

Most healthcare researchers have focused on disease detection (Ayer et al. 2012, Erenay et al. 2014) instead of disease monitoring (Helm et al. 2015). What makes a monitoring problem challenging is the progressive nature of a chronic disease, which demands continuous treatment adjustments. We propose a decision-making framework, which can optimize the appointment frequencies for CKD patients. All inputs to our model come from U.S. Department of Veterans Affairs hospitals. Our CKD database consists of 68,513 patients, treated at eleven Veterans Administration (VA) hospitals, geographically dispersed throughout the United States between January 1, 2009, and February 21, 2016.

We integrate multiple methods, which involve three analytical and empirical approaches. The first is a case-based reasoning (CBR) model (Kolodner 2014). The second is a Cox proportional hazards model (Klein and Moeschberger 2005). The third is a finite-horizon Markov decision process (MDP) model parameterized by outputs from the first two models. The proposed CBR model estimates the transition probability matrix, and the survival model determines the number of days before reaching a terminal state (dialysis or death). The proposed MDP is used to maximize the expected quality-adjusted life days (QALDs) for each patient.

We chose a finite-horizon MDP as it can help doctors make evidence-based and data-driven follow-up appointment decisions, and maximize patient's QALD through nephrologist visits. This is the first MDP-based research that effectively schedules appointments for chronically ill patients to better health outcomes, while reducing unnecessary visits and more efficiently deploying scarce medical resources. The proposed *integrated* MDP (hereafter iMDP) decision framework uses the data on CKD patients to customize policies and determine when a patient should visit the nephrologist next.

The conventional MDP action alternatives in the literature are often binary: *wait* or *visit the doctor today* as shown in Ayer et al. (2012) for breast cancer and Erenay et al. (2014) for colorectal cancer. In the proposed iMDP model, we use the appointment schedule currently recommended by NICE as the action space. Such action space is more sensible as patients are usually assigned a follow-up appointment upon completing a clinic visit. Scheduling at the end of the current visit will help patients plan ahead and facilitate short-term personnel management. As many VA patients are older rural veterans with limited mobility, scheduling ahead can allow them a timely request for transportation assistance to attend their appointments.

We identify the conditions under which it may be desirable to prolong the time between appointments for sicker patients, as palliative care or telemedicine may be more appropriate. Palliative care emphasizes alleviating symptoms and discomfort with the goals of improving quality of life for both the patient and

the family (Davison 2011). Telemedicine has also been utilized as a method for leveraging limited nephrology resources by the VA (Crowley et al. 2017). To understand the effects of our iMDP recommendations, we compare them with the NICE guidelines, which closely mimic current VA practices. The attributes used to describe the health status of a patient are all essential for planning a follow-up appointment. Our model ensures that every patient is seen at least once per year by a nephrologist, a practice not currently enforced by the VA but emphasized by NICE/National Institute for Health and Care Excellence (2014), Stevens and Levin (2013), and Mandal (2015). Although our model is applied to CKD patients, it can be adapted for patients with other chronic conditions. For example, the iMDP can be tailored to provide personalized treatment policies for patients with diabetes or heart failure, because of the similarity in the structure of the data needed to describe a patient's CKD, diabetes, and heart failure progression. All three diseases require doctors to monitor a vector of secondary measures (e.g., blood pressure, weight). Furthermore, the progression of each of the three diseases can be measured with distinct metrics, that is, eGFR for CKD, HbA1c for diabetes, and ejection fraction for heart failure. The information needed to implement iMDP for a different illness includes (i) attributes characterizing the specific chronic disease and (ii) electronic medical records (i.e., *big hospital data*) on the population of interest.

The remainder of the study is organized as follows. Section 2 reviews the literature. In section 3, we propose the iMDP model for chronic disease monitoring. Section 4 parameterizes the iMDP. The numerical results, including an evaluation of the optimal-monitoring settings are presented in section 5. Finally, concluding remarks and future research directions are given in section 6.

2. Literature Review

In this section, we review the literature on CKD management, and then examine MDP models in the healthcare and disease management field.

2.1. CKD Management

Two important OM/OR studies focusing on the treatment of CKD patients are discussed here. First, Lee et al. (2008) develop an approximate dynamic programming model to examine cost effective dialysis initiations and dosage adjustment with the goal of optimizing dialysis patient's wellbeing. They focus on dialysis dose adjustments during check-ups, which occur every 6 months or when the patient experiences an event (i.e., transplant arrival, graft failure, hospitalization). The time until next intervention is not a decision variable.

Skandari et al. (2015) focus on vascular access surgery for patients in need of dialysis. They address whether and when to perform such a surgery on a new or established dialysis patient, in order to maximize life expectancy. Their model incorporates the information of patient's time since dialysis initiation, number of unsuccessful vascular access attempts, and possible attempts left. Similar to Lee et al. (2008), they focus on CKD patients who are in need of dialysis, while our work examines patients before dialysis. Their model considers two action alternatives (1) do nothing, and (2) perform a surgery to provide vascular access for dialysis within a certain time period.

Both Lee et al. (2008) and Skandari et al. (2015) contribute to the literature on optimizing patient's dialysis treatment decisions. In contrast, we are the first to use analytical modelling approaches to address the monitoring process before patients start a dialysis treatment. Designing a monitoring schedule for CKD patients prior to dialysis is crucial as it can help individuals with CKD avoid fast disease deterioration and dialysis initiation. Indeed, most patients die before reaching dialysis (Foley et al. 2005, Keith et al. 2004, Peralta et al. 2006, and Thompson et al. 2015), hence it is important to focus on improving patients' pre-dialysis care.

2.2. Markov Decision Process Models for Healthcare and Disease Management

A MDP model can address the CKD disease monitoring problem, as it tackles uncertainty and sequential decision making (i.e., each decision depends on previous actions taken). MDPs contain four components: (i) a state space (all possible states a patient can fall under), (ii) action alternatives a decision maker can choose from, (iii) transition probabilities (the chance a state transition will occur given the action chosen and the patient's previous state), and (iv) rewards/costs associated with patients' states and actions taken.

MDPs have been applied to healthcare problems from the perspectives of the patients (Alagoz et al. 2004) and the society (Maillart et al. 2008). They have been used to maximize life expectancies (Magni et al. 2000), minimize cost (Lefévre 1981), and optimize policies based on cost and effect analysis (Hauskrecht and Fraser 2000). For example, Gupta and Wang (2008), Patrick et al. (2008), Feldman et al. (2014) have applied MDPs to schedule appointments following patients' requests. In particular, Gupta and Wang (2008) use a MDP for appointment booking by accommodating patients' choice and physician's availability. The MDP by Patrick et al. (2008) allocates capacity to patients to meet wait-time targets in a cost-effective manner, while Feldman et al. (2014) develop a MDP

appointment model to decide which days to open (i.e., make available) for patients to select an appointment. Our iMDP model differs from theirs in its objective and focus. We focus on determining the time intervals between a patient's subsequent visits with the goal of maximizing quality of life, while they assign patients to appointment slots subject to capacity and cost constraints.

During patient's office visit, doctors have limited time to process all patient's data accumulated over time in electronic medical records (EMRs). Thus, comprehensive diagnosis and effective treatment decisions cannot be guaranteed (Hogarth and Makridakis 1981). In fact, there exists a high correlation between decision speed and forecast errors (Moritz et al. 2014); inaccurate disease trajectory predictions often lead to poor treatment choices. MDPs can help doctors effectively use rich patient information stored in EMR and make timely recommendations, that is, clinics can use MDPs parametrized by EMR to improve their performance. MDPs are attractive as they do not need to dichotomize patients into progressors and non-progressors (Helm et al. 2015), thus avoid the need for a subjective judgment call.

Among the MDP-based disease management models, Ayer et al. (2012) adopt a partially observable MDP (POMDP) as the decision maker cannot observe whether the true health state of a patient is 0 (cancer free), 1 (noninvasive cancer), or 2 (invasive cancer) unless a biopsy is performed. Similarly, Erenay et al. (2014) employ a POMDP, as they cannot fully observe whether a patient has no lesion, polyp, or colorectal cancer. Recently, Steimle and Denton (2017) reviewed some MDP optimization models which share goals similar to ours—enhancing chronic disease patient's quality of life. There, Shechter et al. (2008) determine when it is optimal to initiate highly active antiretroviral therapy in HIV patients, and Alagoz et al. (2004) use a MDP to determine when a patient with end stage liver disease should accept a living-donor transplant. Mason et al. (2012) utilize a MDP model to optimize medications prescribed to type 2 diabetes patients. They identify the optimal time to initiate cholesterol and blood pressure lowering medications to maximize the total expected dollar reward prior to death, stroke, or coronary heart disease onset. Finally, Zhang et al. (2012) optimize screening policies for prostate cancer patients to maximize (willingness to pay x quality of life) - (the costs of screening and treatment) over a patient's lifetime.

The above research reviewed by Steimle and Denton (2017) examines problems different from ours, and thus have different action space structures. They allow for two types of settings: *wait* or *act* (occasionally allowing for alternatives such as choosing among medications). Our model has four action alternatives, which have an underlying wait period before an action is initiated (i.e., wait for 1.5, 3, 6, 12 months before seeing the doctor). Our iMDP action alternatives ensure that a patient is scheduled for a follow-up visit at the end of his doctor visit based on his health state. These options available in our iMDP model are consistent with how healthcare providers currently schedule patients at the end of their doctor's office visit.

Table 1 contrasts our iMDP approach with other disease management models discussed above. Similar to some of them, we examine a disease management problem from the patient's perspective and use personalized treatments to enhance quality of life. We set our problem as a discrete-time, finite-horizon MDP, because we know the patient's health state (i.e., CKD stages are determined by eGFR lab results). Our research focuses on optimizing CKD monitoring through quantifying appointment frequency's impact on a patients' quality of life.

In terms of parameterizing their models, researchers have tried simulation (Lee et al. 2008), forecasting (Helm et al. 2015), etc. Our method differs in the generalizability of its components. We use a case-based reasoning (CBR) model (Choudhury and Begum 2016) to parameterize the transition probability matrix of the iMDP. A CBR model projects a patient's disease progression trajectory by using the

Table 1 Disease Management Model

Reference	POMDP	MDP	DP	Personalized care	Chronic disease	Appt. frequency impact
Alagoz et al. (2004)		√		√	√	
Ayer et al. (2012)	√			√		
Erenay et al. (2014)	√			√		
Helm et al. (2015)				√	√	
Lee et al. (2008)			√			
Mason et al. (2012)		√		√	√	
Shechter et al. (2008)		√		√	√	
Skandari et al. (2015)			√	√		
Zhang et al. (2012)	√			√	√	
iMDP Model		√		√	√	√

recorded information of other patients who share the *similar* disease characteristics. Thus, to develop a sound model, researchers need to design a proper measure to identify *similar* patients. Alagoz et al. (2005) propose an opinion-based similarity metric which requires a survey to elicit clinicians' inputs. Instead, we employ a data-mining driven CBR approach (see section 4.1) to identify a cohort of nearest neighbors and project the disease progression of a specific patient. This allows us to apply the iMDP framework to different chronic conditions with minimal physician intervention, as the EMR database of the disease and its characteristics can be automatically fed into our model.

3. Markov Decision Process to Monitor Chronic Kidney Disease

In this section, we detail the iMDP model for CKD monitoring. First, we discuss the state space selection and introduce the notations necessary for our model. Second, we develop the objective functions and propose a finite-horizon discrete-state MDP model to maximize QALDs. The problem is examined from the patient's perspective. Since VA patients are US veterans who do not pay for healthcare, we do not explicitly consider costs. We make the standard MDP assumption that patients are risk neutral. The proposed MDP model will recommend the best timing of patients' follow-up visits contingent on their health state.

3.1. State Space Selection and Model Notations

The model accounts for both the benefits and disutilities associated with appointment attendance. The appointment benefits are implicitly built in the transition probability matrix, which is parameterized using a case based reasoning model (see section 4.1). The model will predict patient's health state i periods from today given his current health state $\mathbf{s}$ and a scheduled follow-up nephrology visit in i epochs. Thus, our MDP can quantify the benefit of seeing a nephrologist i periods from today. On the other hand, including hardship measure of attending an appointment helps quantify the disutility associated with doctor visits. It accounts for the time a patient will spend travelling to and from an appointment and the time he will spend at the nephrologist office (waiting for the doctor and being examined). Please refer to section 4.3.2 and Appendix A, for more information on the hardship metric and its parameterization.

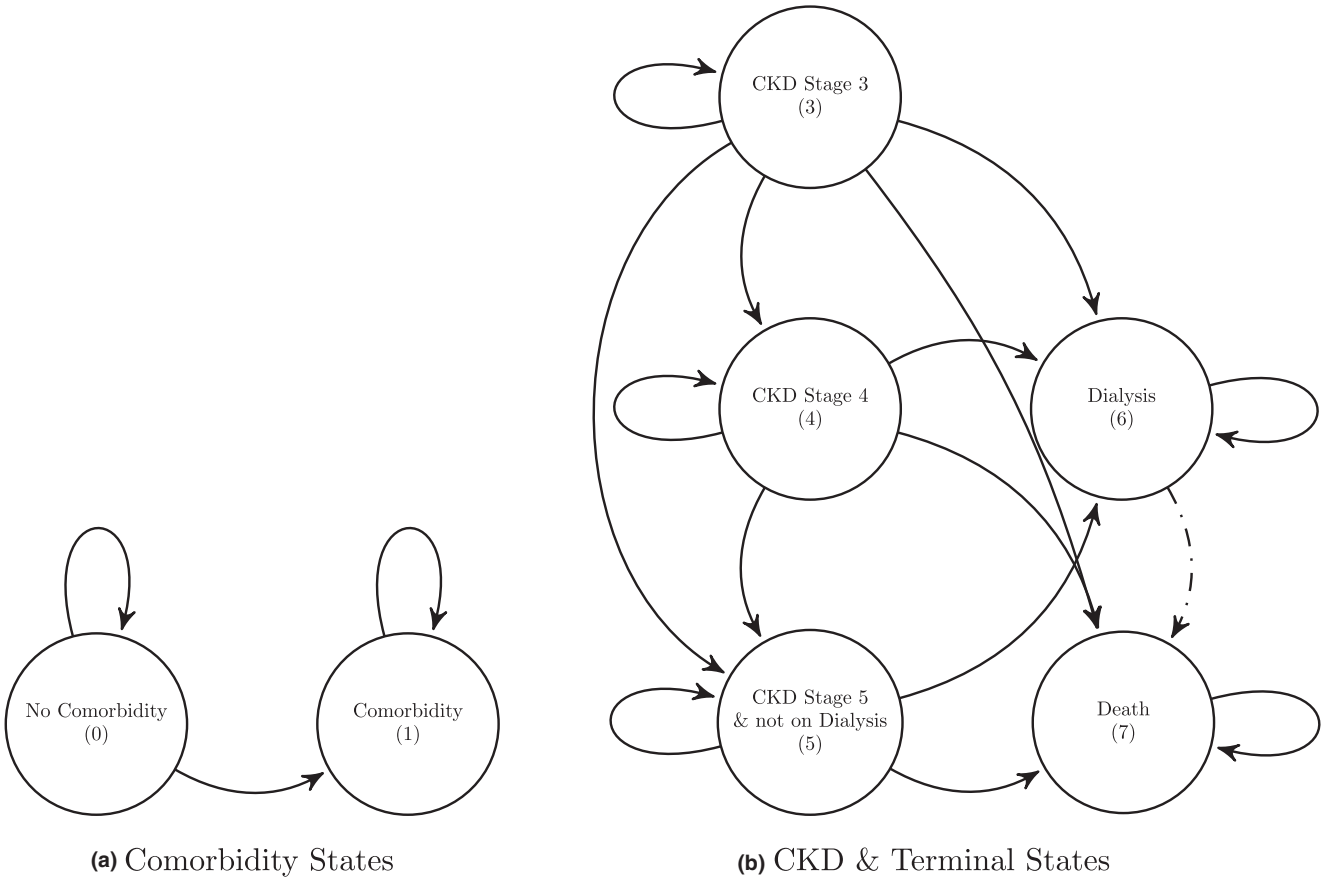
The MDP considers four appointment options: visit the doctor in 1.5, 3, 6, or 12 months, which are the choices NICE currently offers (Mandal 2015, NICE/National Institute for Health and Care Excellence 2014, Stevens and Levin 2013). NICE recommends a fixed time interval between successive appointments for a patient, depending on his CKD Stage. The NICE guidelines are similar to those suggested by KDIGO, a global nonprofit organization that offers evidence-based clinical guidelines for kidney disease. It suggests that at kidney disease onset (i.e., when a patient's health status is relatively stable), PCPs are the primary caregivers. As the disease progresses, patients should visit a nephrologist (Inker et al. 2014). Such visits could occur once every 6–12 months for CKD Stage 3 patients, every 3–6 months for Stage 4 patients, and more frequently for Stage 5 patients (VA/Department of Veterans Affairs 2008, pp. 67). In contrast, our model establishes a dynamic appointment schedule where the time between visits is not constant but depends on a patient's health status, which includes many components such as age, CKD Stage, and different comorbidities. According to the CDC data, CKD incidences increase significantly for individuals over 60 years of age (82% of the CKD patients). Thus, for veterans (often older individuals) we focus on individuals between the ages of 60 and 90.

In this research, we take into account if patients have common CKD comorbidities: diabetes, vascular disease (peripheral or cardiovascular), and heart failure. In line with the literature, we assume comorbidities cannot be cured (Baumgartner et al. 2005, Nair et al. 2020, Smith 1985). Figure 1a shows that a patient without a comorbidity (in state 0) can either remain in the same state (stay in state 0) or transition to state 1 (develop a comorbidity). An individual with a comorbidity (in state 1) cannot leave that state.

We study veterans with moderate to severe chronic kidney disease (CKD Stages 3–5), as their care is more demanding and CKD Stages 1–2 are often not diagnosed (NIH/National Institutes of Health 2012). We use the patient's eGFR data recorded at each doctor visit to determine his CKD Stage. Kidney disease cannot be reversed—it can only stabilize or advance (Eddy 2005). The kidney disease state transitions are shown in Figure 1b, where a patient in state 3 (see the value **3** inside the parentheses in the top circle) may stay in state 3 or transition to a more advanced state. Once a patient moves to state 4, he may stay there or transition to state 5, 6, or 7, but cannot go back to state 3. The same is true for state 5 patients. Once a patient enters state 6 (dialysis) or 7 (death), he will stay there as both are terminal states. State 6 is considered terminal in our research as it requires different care resources. Prior to dialysis, patients will visit a standard nephrology clinic; once dialyzed, they transition to a dialysis clinic.

We focus on patient care prior to reaching the dialysis stage, as such patients can benefit from visiting nephrologists to slow or stabilize CKD deterioration. Optimizing the care for patients prior

Figure 1 State Space



(a) Comorbidity States **(b)** CKD & Terminal States

to dialysis is important as it affects a significant number of CKD patients, and many pass away without transitioning to dialysis (Foley et al. 2005, Keith et al. 2004, Peralta et al. 2006, and Thompson et al. 2015). Since both dialysis and death are terminal states and dialysis patients visit dialysis facilities not regular nephrologists, we do not study the transition from state 6 to state 7 (the directed dash line in Figure 1b).

The notations necessary for our model are listed in Table 2. We first define our decision epochs ($n \in \{1, \ldots, N\}$) and identify all components of the state space ($\mathbf{S}$). We also list the parameters pertaining to the action space, and the transition probability matrix. Finally, we specify the reward parameters and the value function notation. Figure 2 shows how the parameters in Table 2 are interrelated and how they are aggregated to obtain the immediate and terminal (i.e., period-N) reward functions, as well as the iMDP value function. Details are given in section 3.2.

Our model accounts for the possibility that while waiting for an appointment, a patient may experience an observable complication, which could result in death or dialysis initiation. If no sudden deterioration occurs, a patient will not go to an Emergency Room (ER) and will wait until the next scheduled visit. We use "No ER" in Figure 3 to mark the alternative associated with following the schedule recommended by our model. Note that $i = 1$, $i = 2$, $i = 4$, $i = 8$ correspond to visiting a doctor in 1.5, 3, 6, and 12 months, respectively. The "No ER" branches are associated with the non-terminal states, while the "Dialysis" and "Death" branches are associated with the terminal states.

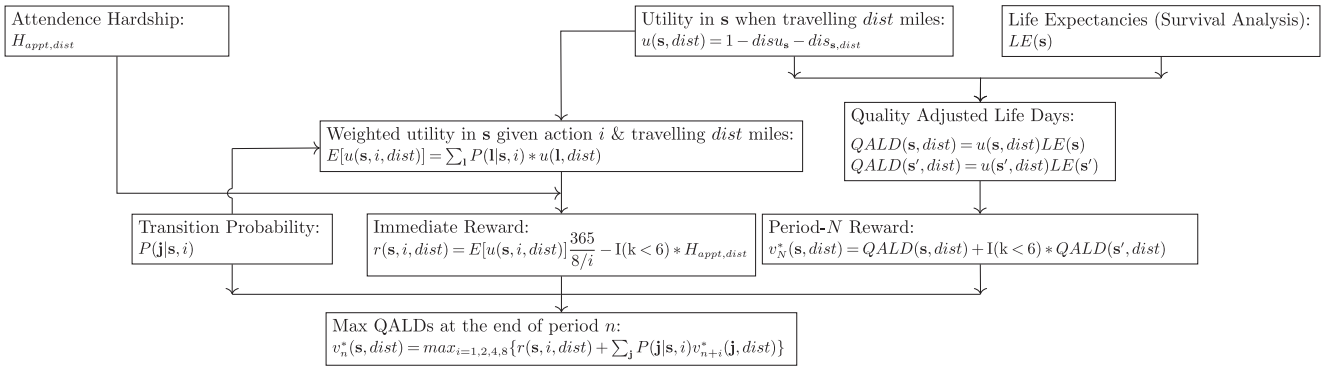
3.2. Formulating the MDP Objective Function

We now develop the period-N reward (i.e., $v_N^*(\mathbf{s}, dist)$ equation below) of the finite horizon MDP. It is the patient's expected QALDs at the end of the planning horizon N, given that the patient is in state $\mathbf{s}$ at period N. The period-N reward, $v_N^*(\mathbf{s}, dist)$, is estimated using life expectancies ($LE(\mathbf{s})$, obtained through survival analysis) and adjusted by patient's utility metrics ($u(\mathbf{s}, dist) = 1 - disu_{\mathbf{s}} - disu_{\mathbf{s},dist}$), which is a function of the patient's health state $\mathbf{s}$ and his distance proximity ($dist$) from his nephrologist. The disutility measures are collected from medical

Table 2 Model Notations

Decision Epoch	N	length of time horizon, $N < \infty$
	n	time index ($n \in \{1, \ldots, N\}$)
State Space	d	diabetes indicator variable ($d = 0$: does not have diabetes; $d = 1$: has diabetes)
	h	heart failure (HF) indicator variable ($h = 0$: does not have HF; $h = 1$: has HF)
	v	vascular disease (VD) indicator variable ($v = 0$: does not have VD; $v = 1$: has VD)
	k	CKD indicator variable ($k = 3$: CKD Stage 3; $k = 4$: CKD Stage 4; $k = 5$: CKD Stage 5; $k = 6$: dialyzed; $k = 7$: death)
	age	patient's age ($age \in \{60, \ldots, 90\}$)
	$\mathbf{s}$	health state, where $\mathbf{s} = (d, h, v, k, age)$
	$\mathbf{s}'$	dialysis health state, where $\mathbf{s}' = (d', h', v', 6, age')$
	$\mathbf{S}$	the state space ($\mathbf{s} \in \mathbf{S}$)
Action Space	i	action i (seeing a doctor in $i * 1.5$ months, e.g., $i = 8$—seeing a doctor in $8 * 1.5 = 12$ months)
	$\mathbf{A}$	action space
Transition Probability	$P(\mathbf{j} \mid \mathbf{s}, i)$	the *probability* of transitioning from state $\mathbf{s}$ to state $\mathbf{j}$ given that action i is chosen
	$\mathbf{P}(\cdot \mid \mathbf{s}, i)$	a *vector*, which specifies the probabilities of transitioning from state $\mathbf{s}$ to any state in $\mathbf{S}$, given that action i is chosen
	$\mathbf{P_i}$	the transition probability *matrix* associated with action i
Reward Parameters	$disu_{\mathbf{s}}$ (see Equation 2)	the disutility associated with being in state $\mathbf{s}$
	$disu_{\mathbf{s},dist}$ (see Equation 3)	the disutility associatedwith being in state $\mathbf{s}$ and travelling *dist* miles to see a nephrologist
	$H_{appt,dist}$ (see Equation 4)	the hardship from the travel (*dist*) and waiting time, and nephrology appointment duration
	$u(\mathbf{s}, dist)$	the utility associated with being in state $\mathbf{s}$ and travelling *dist* miles to see a nephrologist, where $u(\mathbf{s}, dist) = 1 - disu_{\mathbf{s}} - disu_{\mathbf{s},dist}$ and $u(\mathbf{s}, dist) = 0$ if $k = 7$
	$LE(\mathbf{s})$	the life expectancy of a patient in state $\mathbf{s}$
	$QALD(\mathbf{s}, dist)$	the quality adjusted life days of a patient in state $\mathbf{s}$, who travels *dist* miles to see a nephrologist, where $QALD(\mathbf{s}, dist) = u(\mathbf{s}, dist)LE(\mathbf{s})$
	$E[u(\mathbf{s}, i, dist)]$	the weighted utility given that a patient in state $\mathbf{s}$, who travels *dist* miles to see a nephrologist, is scheduled using appointment policy i, where $E[u(\mathbf{s}, i, dist)] = \sum_{\mathbf{l}} P(\mathbf{l} \mid \mathbf{s}, i) * u(\mathbf{l}, dist)$
	$r(\mathbf{s}, i, dist)$ (see Equation 1a)	the immediate reward given that a patient is in state $\mathbf{s}$, who travels *dist* miles to see a nephrologist, is scheduled using appointment policy i; ($\mathrm{I}(k < 6) = 1$ if $k < 6$ and $\mathrm{I}(k < 6) = 0$ if $k \geq 6$) $r(\mathbf{s}, i, dist) = E[u(\mathbf{s}, i, dist)]\frac{365}{8/i} - \mathrm{I}(k < 6) * H_{appt,dist}$
Value Funct.	$v_n^*(\mathbf{s}, dist)$ (see Equation 1)	the maximum expected QALDs at period n when the patient is in state $\mathbf{s}$ and has travelled *dist* distance to see a nephrologist

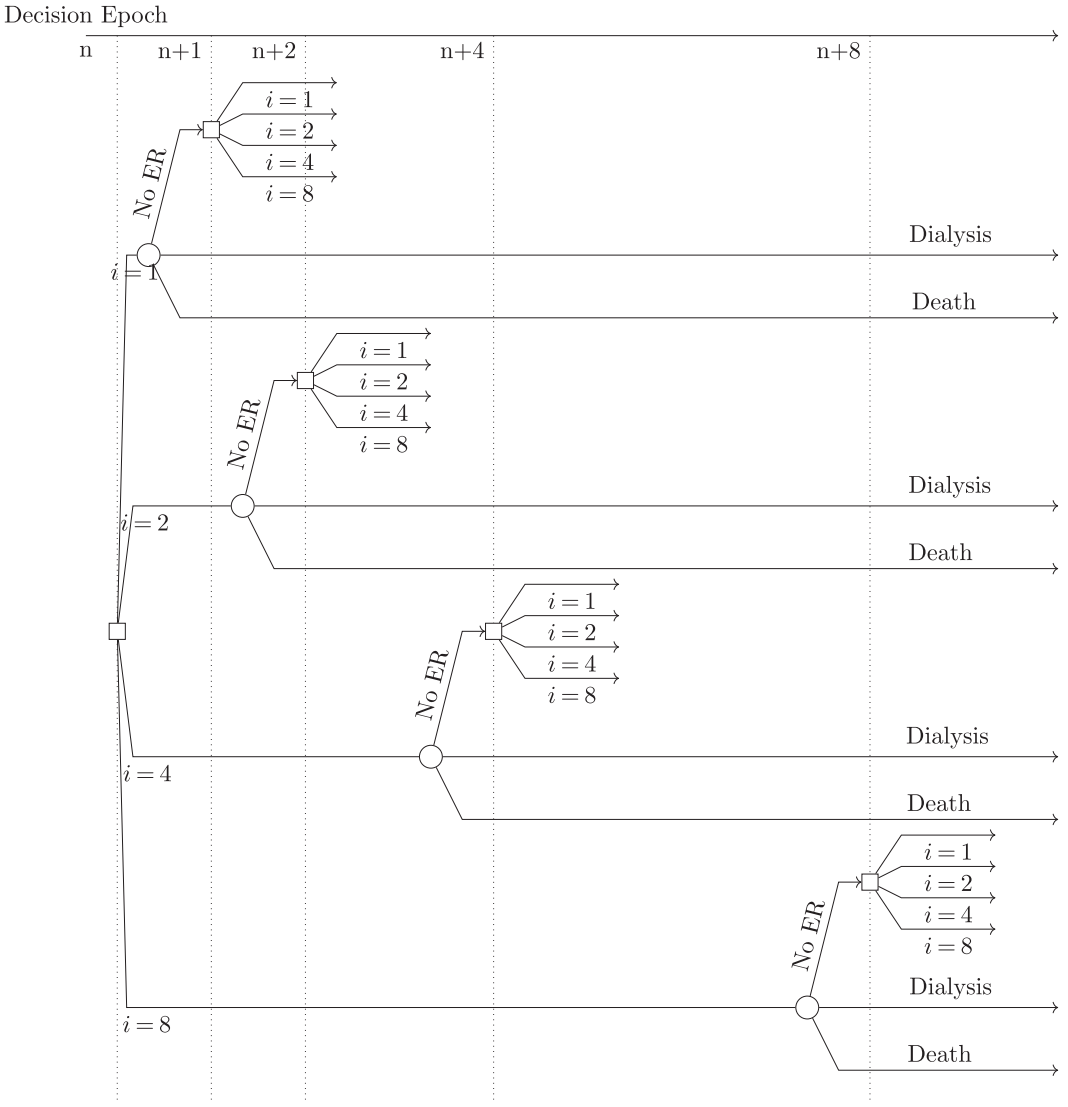
Figure 2 A Detailed Illustration of the Relationships Among the Notations Defined in Table 2



journal publications (see Table A1). For patients not currently on dialysis, $v_N^*(\mathbf{s}, dist)$ has two components ($QALD(\mathbf{s}, dist)$ and $QALD(\mathbf{s}', dist)$). The first indicates the quality expected life days ($QALD(\mathbf{s}, dist)$) prior to dialysis given the patient's current state ($\mathbf{s}$). The second denotes the quality of expected life days ($QALD(\mathbf{s}', dist)$) if the patient transitions from state $\mathbf{s}$ to state $\mathbf{s}'$ (i.e., dialysis state). The second component will not exist if a patient is already on dialysis ($k = 6$) and stays on dialysis. Finally, all patients who are dead ($k = 7$) have an overall quality of life equal to 0.

$$
\begin{aligned}
v_N^*(\mathbf{s}, dist) &= \begin{cases} (1-disu_{\mathbf{s}}-disu_{\mathbf{s},dist}) * LE(\mathbf{s}) + (1-disu_{\mathbf{s}'}-disu_{\mathbf{s}',dist}) * LE(\mathbf{s}') & \text{if } k<6 \\ (1-disu_{\mathbf{s}}-disu_{\mathbf{s},dist}) * LE(\mathbf{s}) & \text{if } k=6 \\ 0 & \text{if } k=7 \end{cases} \\
&= \begin{cases} u(\mathbf{s}, dist) * LE(\mathbf{s}) + u(\mathbf{s}', dist) * LE(\mathbf{s}') & \text{if } k<6 \\ u(\mathbf{s}, dist) * LE(\mathbf{s}) & \text{if } k=6 \\ 0 & \text{if } k=7 \end{cases} \\
&= \begin{cases} QALD(\mathbf{s}, dist) + QALD(\mathbf{s}', dist) & \text{if } k<6 \\ QALD(\mathbf{s}, dist) & \text{if } k=6 \\ 0 & \text{if } k=7 \end{cases} \\
&= QALD(\mathbf{s}, dist) + \mathrm{I}(\mathrm{k}<6) * QALD(\mathbf{s}', dist).
\end{aligned}
$$

Figure 3 The Logic Flow of the Decision Process



The value function $v_n^*(\mathbf{s}, dist)$ in Equation 1 represents the maximum total expected QALDs in period n ($n = 1, \ldots, N-1$), when the patient is in state $\mathbf{s}$ and his proximity to a nephrologist is *dist*:

$$v_n^*(\mathbf{s}, dist) = max_{i=1,2,4,8}\{r(\mathbf{s}, i, dist) + \sum_{\mathbf{j}} P(\mathbf{j}|\mathbf{s}, i) v_{n+i}^*(\mathbf{j}, dist)\}. \quad (1)$$

The immediate reward function ($r(\mathbf{s}, i, dist)$) provides the QALDs until the next appointment given that the patient is in state $\mathbf{s}$, chooses appointment timing i, and travels *dist* to see his nephrologist. Equation (1) shows that $r(\mathbf{s}, i, dist)$ depends on four sets of parameters: (1) the disutilities associated with being in state $\mathbf{s}$ (i.e., $disu_{\mathbf{s}}$), (2) the disutility associated with being in state $\mathbf{s}$, and living *dist* miles away from the nephrologist (i.e., $disu_{\mathbf{s},dist}$), (3) the probability of transitioning from state $\mathbf{s}$ to state $\mathbf{j}'$ as a result of choosing action i (i.e., $P(\mathbf{j}'|\mathbf{s}, i)$, and (4) the hardship associated with travelling to and attending an appointment (i.e., $H_{appt,dist}$). Thus, in Equation (1a) we show that the immediate reward $r(\mathbf{s}, i, dist)$ accounts for (1) the weighted utility of being in state $\mathbf{s}$, selecting action i and living *dist* away from a nephrologist ($E[u(\mathbf{s}, i, dist)]$); (2) the time between the current and next appointment, which depends on the action i taken ($\frac{365}{8/i}$); and (3) whether the patient is in a non-terminal state ($k < 6$) as that determines if he is attending nephrology clinic appointments and accruing an attendance hardship ($H_{appt,dist}$).

$$\begin{aligned} r(\mathbf{s}, i, dist) &= \begin{cases} \sum_{\mathbf{j}'} P(\mathbf{j}'|\mathbf{s}, i) * (1 - disu_{\mathbf{j}'} - disu_{\mathbf{j}',dist}) * \frac{365}{8/i} - H_{appt,dist} & \text{if } k<6 \\ \sum_{\mathbf{j}'} P(\mathbf{j}'|\mathbf{s}, i) * (1 - disu_{\mathbf{j}'} - disu_{\mathbf{j}',dist}) * \frac{365}{8/i} & \text{if } k=6 \\ 0 & \text{if } k=7 \end{cases} \\ &= \begin{cases} \sum_{\mathbf{j}'} P(\mathbf{j}'|\mathbf{s}, i) * u(\mathbf{j}', dist) * \frac{365}{8/i} - H_{appt,dist} & \text{if } k<6 \\ \sum_{\mathbf{j}'} P(\mathbf{j}'|\mathbf{s}, i) * u(\mathbf{j}', dist) * \frac{365}{8/i} & \text{if } k=6 \\ 0 & \text{if } k=7 \end{cases} \\ &= E[u(\mathbf{s}, i, dist)]\frac{365}{8/i} - \mathrm{I}(\mathrm{k}<6) * H_{appt,dist.} \end{aligned} \quad (1a)$$

Thus, if our time horizon $N = 8$ and the model selects the $i = 1 \to i = 2 \to i = 1 \to i = 4$ policy, we would accumulate $r_1 \to r_2 \to r_1 \to r_4$ immediate rewards. We have highlighted the policy in Table 3. Each row in the table represents a different epoch. For example, e_0 is the current epoch, e_8 is the epoch eight periods (i.e., 12 months) into the future. The columns represent the four alternative actions (i.e., $i = 1$, $i = 2$, $i = 4$ and $i = 8$). The values inside the table indicate the epoch a patient will transition into if he chooses the action indicated in the column header. For instance, if a patient is in time e_0 and chooses action $i = 1$ ($i = 8$) he will see the doctor in epoch e_1 (e_8). In Table 3, we use the solid blue arrows to highlight the sample path and show the epoch transition driven by the policy. The dashed arrows point to the epoch row we should continue with given the observed epoch transition. Following the $i = 1 \to i = 2 \to i = 1 \to i = 4$ policy, the patient will first transition from epoch e_0 to e_1 (solid arrow) and move to row e_1 (dashed arrow) which serves as the next starting point. This policy indicates that the MDP recommends seeing a patient in one epoch (i.e., one epoch = 1.5 months) from today. Note that actions are dependent on the length of the time horizon. For example, in Table 3, $i = 8$ is only feasible in epoch e_0 (the 1^{st} row). When the planning horizon is one year (8 epochs) and the stating time is greater than e_0, the patient's visit date will exceed the planning horizon (i.e., $N = 8$). Thus, action $i = 8$ cannot be selected in epoch 1, as $1 + 8 = 9$ indicating the appointment will take place in epoch 9, which is beyond the planning horizon ($N = 8$) shown in this figure.

4. Parameterizing the iMDP Model

In this section, we introduce the unified research framework and derive the inputs to parameterize the iMDP. Figure 4 gives the iMDP framework, which contains two components: modeling and clinical management knowledge. First, we will discuss the modelling components, which consist of the CBR (section 4.1) and Survival Analysis (section 4.2) models. Second, we will review the literature pertinent to parameterizing our iMDP (section 4.3).

Table 3 Policy $a_1 \to a_2 \to a_1 \to a_4$ Example

	$i=1$	$i=2$	$i=4$	$i=8$
e_0	e_1	e_2	e_4	e_8
e_1	e_2	e_3	e_5	
e_2	e_3	e_4	e_6	
e_3	e_4	e_5	e_7	
e_4	e_5	e_6	e_8	
e_5	e_6	e_7		
e_6	e_7	e_8		
e_7	e_8			
e_8				

4.1. CBR Model

We now focus on developing a CBR model (Richter and Weber 2016) to predict patients' CKD progression. The proposed CBR employs a machine-learning approach to estimate the iMDP transition probability matrix ($\mathbf{P_i}$). It can be adapted to accommodate the intermittent, multivariate, and correlated patient time series. Disease trajectories vary significantly across patients. Conventional data mining methods use large datasets to derive the relationship between health status trajectories and patient characteristics to predict disease progression. CBRs recognize that a universally applicable equation, which can accurately predict the progression of a patient with an uncommon disease trajectory, is hard to establish. Thus, the proposed CBR predicts a new patient's disease progression using only the medical records of individuals who resemble the patient in question.

CBRs contain old cases, which contain patients' characteristics (referred to as *features*) and disease progressions. The new patient (referred to as a *target*) is compared to all cases in the case-base, and thousands of similar cases are identified and considered when predicting the target's progression. The target and its similar cases share compatible disease progression trajectories, since they have comparable features.

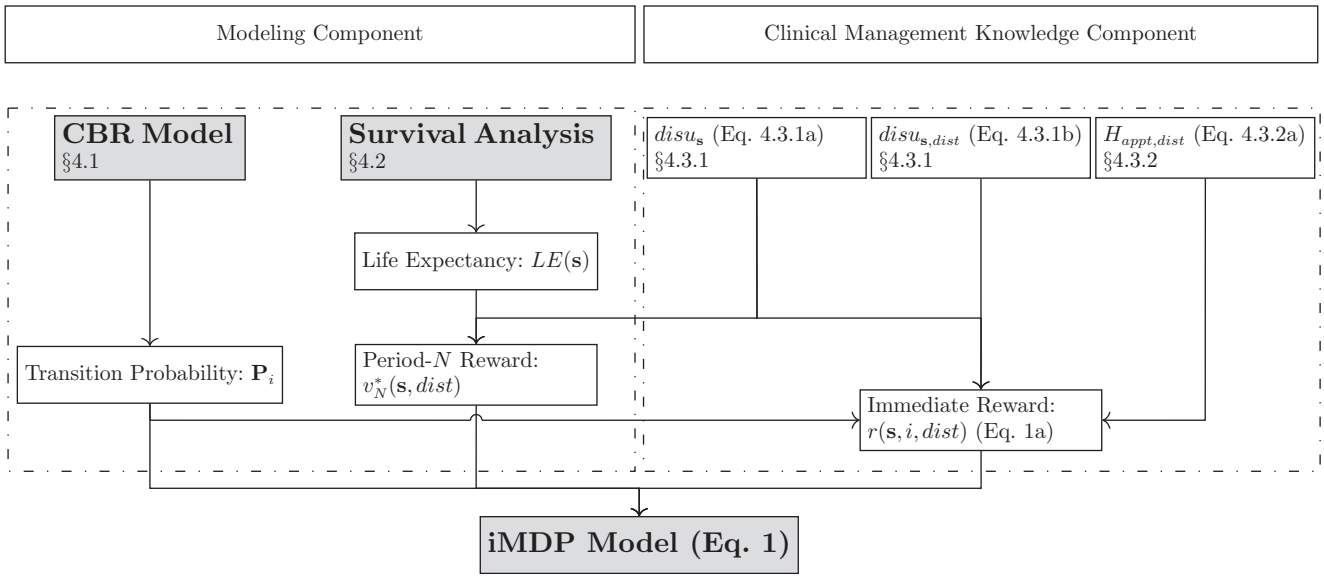
In the CBR model, we convert the patient-level data into cases. Data conversion is necessary to compare the target and its similar cases. Specifically, we let each case contain 12 months of data (Mandal 2015, NICE/National Institute for Health and Care Excellence 2014, Stevens and Levin 2013). A patient's medical records over years can be divided into several cases depending on the length of his historical information. We use a sliding window technique to create multiple cases for patients with more than one year of data. For example, for a patient with 14-month records, we can create three cases based on the data in months 1~12; 2~13; and 3~14.

We propose a machine learning selection procedure a variation of which is discussed in details in Nenova and Shang (2021). First, all CBR cases are filtered so their (1) comorbidities match the target's comorbidities and (2) follow-up appointment frequencies match the iMDP action policy the target would follow (i). The filtering criteria are chosen as patients with different comorbidities and monitoring regimens (i.e., doctor visits) are expected to undergo different disease progressions. For example, the health trajectory of a patient with diabetes and heart failure, seen by a nephrologist in 6 months will likely differ from that of an individual with no comorbidities who will attend a nephrology appointment in a year.

Once the filtered CBR cases are identified, we calculate their closeness to the target. We use Euclidian and dynamic time warping (Zhu et al. 2021) metrics to measure the proximity of the filtered CBR cases to the target. We compute the Euclidean distance for all numerical features except for the time series ones, which are compared using the dynamic time warping metric. The distance between the target and the filtered CBR case c in feature j is labeled as $d_{c,j}$. The distance measures are uniformized, that is, $u_{c,j} = \frac{d_{c,j} - min_c(d_{c,j})}{max_c(d_{c,j}) - min_c(d_{c,j})}$, due to magnitude differences across features. Next, we use a dominance analysis model to calculate the importance weight (imp_j) of each feature j (Moutinho and Hutcheson 2011) and rank all filtered CBR cases based on their weighted average uniform distance to the target ($u_c = \sum_j imp_j u_{c,j}$). Finally, we select the n closest ranked cases (referred to as *solution cases*). Most CBR models use a pre-determined sample size (i.e., fixed number of solution cases) for each target. In contrast, we use a machine learning technique to determine the proper number of cases (n) necessary to project the target disease progression.

As the disease trajectories of all solution cases are known, we use their weighted average trajectory to estimate the expected disease progression of the target. We weight the disease trajectory of each solution case c based on its overall uniform distance to the target $\left(w_c = \frac{1/u_{[c]}}{\sum_c (1/u_{[c]})}\right)$. The model's performance across three dependent variables (i.e., eGFR, dialysis, and death) has been compared with that of a variety of

Figure 4 iMDP for Identifying the Best Follow-up Appointment Time



time series and data mining models. We found the proposed CBR outperforms all standard modeling techniques.

Using the CBR model, we forecast the state of the *target i* epochs into the future, given that he starts in state **s** and follows appointment policy *i*. The number of *targets* who start in state **s** and reach state **j** after following action *i* are denoted as $F(\mathbf{j}|\mathbf{s}, i)$. The probability of a patient transitioning from state **s** to state **j** following action *i* is defined as $P(\mathbf{j}|\mathbf{s}, i) = F(\mathbf{j}|\mathbf{s}, i)/F(\mathbf{s})$, where $F(\mathbf{s})$ is the total number of *targets* who start in state **s**. For example, 463 of our target patients were in state **s**: 64 years old in CKD Stage 3 with 0 comorbidities, that is, **s** = {diabetes, heart failure, vascular disease, CKD, age} = {d, h, v, k, age} = {0, 0, 0, 3, 64}. After following policy $i = 8$, 401 of them were found to be in the same state (but one year older, i.e., 65 years old), 32 were forecasted to transition to CKD Stage 4 with 0 comorbidities (**j**). Therefore, $P(000365|000364, 8) = 401/463 = 0.8661$; $P(000465|000364, 8) = 0.0691$.

4.2. Survival Analysis Model

We use survival analysis to estimate the time until death or dialysis for a patient currently in state **s** as it has been designed to model censored data (i.e., not all of the patients in our dataset have died or began dialysis). The model determines a patient's life expectancy in days ($LE(\mathbf{s})$), which is used to predict the iMDP's period-N reward ($v_N^*(\mathbf{s}, dist)$), that is, the total remaining QALDs at the end of period N given patient's state and proximity to nephrology care.

We examine four accelerated failure time parametric (Weibull, Exponential, Log-Normal, and Log-Logistic) and one proportional hazards semi-parametric (Cox proportional hazards (PH)) methods. These five alternatives are selected because they are among the most popular survival models. Readers are referred to sections 2.1 and 2.3 in Seetharaman and Chintagunta (2003) for details on the Cox PH model and parametric baseline hazard specifications.

Survival models predict the time until event for a patient given his initial health status information. Unlike the CBR model in section 4.1, we use patient- rather than case-level data to select a survival model. The predictors are based on a patient's first year data, which is referred to as his baseline year. They include indicator variables specifying whether the patient is diagnosed with diabetes, heart failure, and vascular disease during his baseline year. To categorize an individual's CKD Stage we obtain his eGFR records collected during the baseline year. Recall that patients are assigned to CKD Stage 3 if their eGFR $\in [30, 60)$, Stage 4 if their eGFR $\in [15, 30)$, and Stage 5 if their eGFR $\in (0, 15)$. Finally, we record the age at the end of the baseline year and the hospital visited by each patient. Our iMDP has two terminal states: death and dialysis. Thus, the survival analysis models examined are competing risk models, which estimate the time after the baseline year until a terminal event is observed. 1,010 of the 68,513 patients are removed as they have <1 year of data needed for the baseline definition. We discard 22,116 patients, as they are in CKD Stage 1 or 2, and our iMDP model is designed for patients with more advanced kidney disease (Stages 3–5). Hence, our survival analysis dataset contains 45,387 patients.

To compare our models, we randomly pick 90% of the data as a training set (40,849 patients) and use the remaining 10% as a test set (4,538 patients). Four standard survival analysis evaluation metrics are

employed: AIC, BIC, log-likelihood (Lambrecht and Tucker 2013, Sunder et al. 2017), and concordance (Harrell et al. 1996, Pencina and D'Agostino 2004). Columns 3 through 7 (note that column 8 will be discussed below) in Table 4 summarize the models where the time until dialysis and death are predicted using information on patient's comorbidities (diabetes, heart failure, and vascular disease), CKD Stage (where Stage 3 was the baseline) and age. The Cox Proportional Hazards Model 1 has the lowest AIC and BIC, the highest log-likelihood and a comparable concordance. Therefore, it dominates the parametric models across all evaluation metrics.

Furthermore, we examine whether incorporating provider's heterogeneity, measured by hospitals' locations, improves the Cox model prediction capabilities. We use 10 indicator variables to represent the eleven hospital locations. To simplify the results in Table 4, we only specify whether Hospital Location indicators are present (Yes) or absent (No) in the model examined. The two Cox PH models are very compatible (see Columns 7 and 8 in Table 4); we find only one hospital indicator variable is significant. We thus conclude that the best model is Cox PH Model 1. Table 5 shows that the coefficients of the training (40,849 patients) and the full (45,387 patients) datasets are comparable, indicating that the Cox PH Model 1 is stable. Therefore, we use the full dataset Cox PH Model 1 to predict patients' period-N rewards for the iMDP.

4.3. Clinical Management Knowledge

The CBR and survival analysis above have used the VA data to parameterize the iMDP. We now focus on the parameters obtained from recently published research studies. The parameters were chosen after thorough literature review and approved by a consulting nephrologist. We will briefly discuss the disutility (section 4.3.1) and hardship (section 4.3.2) measures here. Detailed information can be found in Appendix A.

4.3.1. Disutility Estimates. We consider two *health-state*-related disutility measures. The first one is dependent on the patient's health status (i.e., $disu_{\mathbf{s}}$). The second accounts for the interaction effect between patient's health status ($\mathbf{s}$) and nephrologist proximity ($dist$) (i.e., $disu_{\mathbf{s},dist}$). These two measures can be viewed as the percentage time lost due to having a chronic condition, being in a certain age group and travelling a specific distance to attend an appointment. They are used to define $u(\mathbf{s}, dist) = 1 - disu_{\mathbf{s}} - disu_{\mathbf{s},dist}$.

Health State Disutilities ($disu_{\mathbf{s}}$): Following Sullivan and Ghushchyan (2006), we assume that to obtain the full disutility of a patient's state we should not only add up the disutility associated with each state feature (i.e., diabetes—d, heart failure—h, vascular disease—v, CKD Stage—k, and age), but also account for the number of patient's coexisting conditions (i.e., $count$) as their interaction affects one's overall health status:

$$disu_{\mathbf{s}} = disu_d + disu_h + disu_v + disu_k + disu_{age} + disu_{count}. \tag{2}$$

Health State and Proximity Disutilities ($disu_{\mathbf{s},dist}$): Researchers have found that there exists a quantifiable discrepancy in treatment outcomes between rural and urban CKD patients, both prior to (Rucker et al. 2011) and after (Tonelli et al. 2006, 2007) dialysis initiation. They maintain that rural patients attend significantly fewer specialist appointments, which could explain the higher mortality and hospitalization rates, and fewer laboratory tests performed and medications prescribed. Similar discrepancies are observed within the VA health system (Tan et al. 2018), where Buzza et al. (2011) report that the top three non-monetary barriers to receiving care are the (1) distance to drive, (2) time, and (3) limited transportation.

To quantify this barrier to care as a joint function of the patient's health state and proximity (i.e., distance) to a doctor ($disu_{\mathbf{s},dist}$), we surveyed the literature (see the middle of Table A1 in Appendix A) on how distance to care affects patients' quality of life. Similar to estimating $disu_{\mathbf{s}}$, we add the disutilities associated with having each chronic condition while travelling $dist$ miles to attend a doctor's appointment. After a careful literature review, we found that medical researchers (1) examined the impact of distance on a patient with heart failure and vascular disease together, which is why we have done the same ($disu_{(h,v),dist}$), and (2) did not consider the joint effect of comorbidity count and proximity to nephrology care on one's health-state disutility, which is why we do not include a $count$ component in our $disu_{\mathbf{s},dist}$ measure below.

$$disu_{\mathbf{s},dist} = disu_{d,dist} + disu_{(h,v),dist} + disu_{k,dist}. \tag{3}$$

4.3.2. Appointment Attendance Hardship ($H_{appt,dist}$). In addition to the disutility measures discussed above, we calculate the expected hardship caused by attending nephrology appointments. We incorporate three appointment attendance hardships. The first accounts for the wait time at the clinic before seeing a nephrologist (wt_{appt}). The second quantifies the expected length of the nephrology appointment (at_{appt}). The last component incorporates the time lost in travelling to and from the doctor's office (dt), which can be particularly problematic for a rural patient attending a nephrology office often located in a

Table 4 Survival Models—Training Set Data

Outcome		Weibull	Exponential	Log-Normal	Log-Logistic	Cox PH Model 1	Cox PH Model 2
Dialysis	Diabetes	−0.9445***	−0.9496***	−0.96***	−0.9672***	0.9561***	0.9134***
		(0.0705)	(0.0673)	(0.0799)	(0.0741)	(0.0673)	(0.0687)
	Heart Failure	−0.4041**	−0.4064**	−0.5661***	−0.4092**	0.4047**	0.4303**
		(0.1699)	(0.1707)	(0.2063)	(0.1898)	(0.1707)	(0.1711)
	Vascular Disease	−0.3748***	−0.3767***	−0.3609***	−0.3733***	0.3738***	0.3957***
		(0.0761)	(0.0761)	(0.0813)	(0.078)	(0.0761)	(0.077)
	Age	0.045***	0.0452***	0.0495***	0.0485***	−0.0449***	−0.045***
		(0.0027)	(0.0024)	(0.0029)	(0.0028)	(0.0024)	(0.0025)
	CKD Stage 4	−2.3211***	−2.334***	−2.5095***	−2.3309***	2.3201***	2.3497***
		(0.0839)	(0.0624)	(0.0834)	(0.0815)	(0.0625)	(0.0629)
	CKD Stage 5	−2.8678***	−2.8832***	−3.4003***	−3.0298***	2.8466***	2.8913***
		(0.1061)	(0.0823)	(0.1184)	(0.1101)	(0.0827)	(0.0862)
	Hospital Location	No	No	No	No	No	Yes
	Training Set AIC	26763.22	26761.28	26651.58	26689.83	22707.53	22678.28
	Training Set BIC	26751.38	26751.17	26639.74	26677.99	22699.11	22651.82
	Training Set Log-likelihood	−13373.61	−13373.64	−13317.79	−13336.91	−11347.76	−11323.14
	Training Set Concordance	0.8449	0.845	0.8455	0.8454	0.8449	0.8503
		(0.0058)	(0.0058)	(0.0058)	(0.0058)	(0.0058)	(0.0058)
	Test Set Concordance	0.5022	0.5022	0.5020	0.5020	0.5023	0.5035
		(0.0085)	(0.008+5)	(0.0085)	(0.0085)	(0.0085)	(0.0084)
Death	Diabetes	−0.2122***	−0.3731***	−0.2276***	−0.2226***	0.4038***	0.4181***
		(0.0278)	(0.051)	(0.0315)	(0.0292)	(0.051)	(0.0515)
	Heart Failure	−0.1957***	−0.3267**	−0.2**	−0.2033***	0.3479***	0.4202***
		(0.0722)	(0.1329)	(0.0845)	(0.0772)	(0.1329)	(0.133)
	Vascular Disease	−0.1716***	−0.2963***	−0.1999***	−0.1852***	0.3077***	0.2824***
		(0.0221)	(0.0405)	(0.0253)	(0.0234)	(0.0405)	(0.0409)
	Age	−0.0192***	−0.0348***	−0.0198***	−0.0198***	0.0348***	0.0365***
		(0.001)	(0.0017)	(0.001)	(0.001)	(0.0017)	(0.0017)
	CKD Stage 4	−0.2274***	−0.34***	−0.2898***	−0.2555***	0.4002***	0.4071***
		(0.0287)	(0.0527)	(0.0327)	(0.0306)	(0.0527)	(0.0529)
	CKD Stage 5	−0.3114***	−0.3831***	−0.3872***	−0.3403***	0.4889***	0.4829***
		(0.0673)	(0.1238)	(0.0713)	(0.0699)	(0.1239)	(0.1246)
	Hospital Location	No	No	No	No	No	Yes
	Training Set AIC	83696.23	81973.81	82172.09	81973.81	79467.46	79170.03
	Training Set BIC	83686.12	83686.12	82160.25	83686.12	79459.04	79143.58
	Training Set Log-likelihood	−41841.12	−40978.91	−41078.04	−40978.91	−39727.73	−39569.02
	Training Set Concordance	0.6137	0.6137	0.6154	0.615	0.6145	0.6181
		(0.0043)	(0.0043)	(0.0043)	(0.0043)	(0.0043)	(0.0043)
	Test Set Concordance	0.4959	0.4962	0.4955	0.4957	0.4960	0.4981
		(0.0046)	(0.0046)	(0.0046)	(0.0046)	(0.0046)	(0.0046)

*$p < 0.10$; **$p < 0.05$; ***$p < 0.001$.

metropolitan area. We add the three measures in our appointment induced hardship to integrate them:

$$H_{appt,dist} = wt_{appt} + at_{appt} + dt. \quad (4)$$

5. MDP Optimal Monitoring Results

We now present the iMDP recommendations, and show how they fare relative to the National Institute for Health and Care Excellence (NICE) guideline and current VA practices. Finally, we conduct an endogeneity check and sensitivity analyses to derive insights.

5.1. iMDP Recommendations

The raw iMDP policy results are presented in Table 6. To visualize the iMDP results and better highlight observations 1 through 5, we aggregate the appointment policies (i's) by averaging the follow-up time according to the CKD and the number of comorbidities (d, h, v). To better explain the outcomes and obtain managerial implications, we summarize them in Figure 5, where we can highlight the iMDP recommendations, NICE guidelines and the VA patients' actual inter-visit times. The differences are apparent and are discussed below.

Table 5 Survival Models—Training and Full Data Sets

Outcome	Predictors	Training set	Full data set
Dialysis	Diabetes	0.9561***	0.9035***
		(0.0673)	(0.0477)
	Heart Failure	0.4047**	0.4699***
		(0.1707)	(0.1185)
	Vascular Disease	0.3738***	0.3321***
		(0.0761)	(0.0556)
	Age	−0.0449***	−0.0457***
		(0.0024)	(0.0017)
	CKD Stage 4	2.3201***	2.3115***
		(0.0625)	(0.045)
	CKD Stage 5	2.8466***	2.8172***
		(0.0827)	(0.0578)
Death	Diabetes	0.4038***	0.3688***
		(0.051)	(0.0363)
	Heart Failure	0.3479***	0.3723***
		(0.1329)	(0.0925)
	Vascular Disease	0.3077***	0.3238***
		(0.0405)	(0.0285)
	Age	0.0348***	0.0374***
		(0.0017)	(0.0012)
	CKD Stage 4	0.4002***	0.4337***
		(0.0527)	(0.0366)
	CKD Stage 5	0.4889***	0.5778***
		(0.1239)	(0.0852)

*$p < 0.10$; **$p < 0.05$; ***$p < 0.001$.

Observation 1 (Actual Appointment Variability). *For a given CKD Stage, the actual appointment variability and patient complexity (i.e., number of comorbidities) are positively correlated.*

Figure 5 shows the time until patient's next nephrologist visit. The vertical line for each comorbidity group is a simplified box plot as it provides the smallest, the average, and the longest time (in epochs, where 1 epoch = 1.5 months) between visits. The intervals reveal the variability inherent in the current VA nephrology appointment schedules. We find the variation in the actual inter-appointment durations (the blue dash-lines' length) increases with the number of comorbidities regardless of the CKD Stage. This increase is most pronounced for CKD Stage 5 patients with three comorbidities (the sickest individuals), which indicates that the current practice for complex patients is highly erratic, that is, some patients visit a nephrologist very often and others very rarely. Therefore, doctors would benefit from additional guidance in deciding on appointment schedules to better serve their patients.

Observation 2 (Early Prevention Focus). *The iMDP recommends significant increases in appointment frequencies for patients in CKD Stage 3.*

Figure 5 suggest that all patients in CKD Stage 3, would benefit from a shorter inter-visit duration (i.e., more frequent appointments). This is consistent with past medical research, which finds that early aggressive treatments can benefit patients in the long-run. For example, highly cited articles have concluded that early aggressive treatment can reduce the rate of kidney deterioration (Parving et al. 1983) and improve the survival of heart disease patients (Mehta et al. 2009). The current long inter-visit durations for CKD Stage 3 patients may be due to limited nephrologists on staff, thus forcing doctors to prioritize their cases. As the iMDP does not consider any provider capacity constraints, it focuses on enhancing QALDs and meeting patients' needs. Figure 5 labels the current practices as *Actual*. The proposed iMDP takes into account the impact of each action and selects the most effective monitoring strategy for every patient. Thus, if CKD Stage 3 patients are seen less frequently due to limited nephrologists' availability the iMDP can be used to justify the need for a capacity expansion (i.e., hiring more physicians).

Observation 3 (NICE Guidelines). *The NICE guidelines are overly demanding for patients with zero or one comorbidity.*

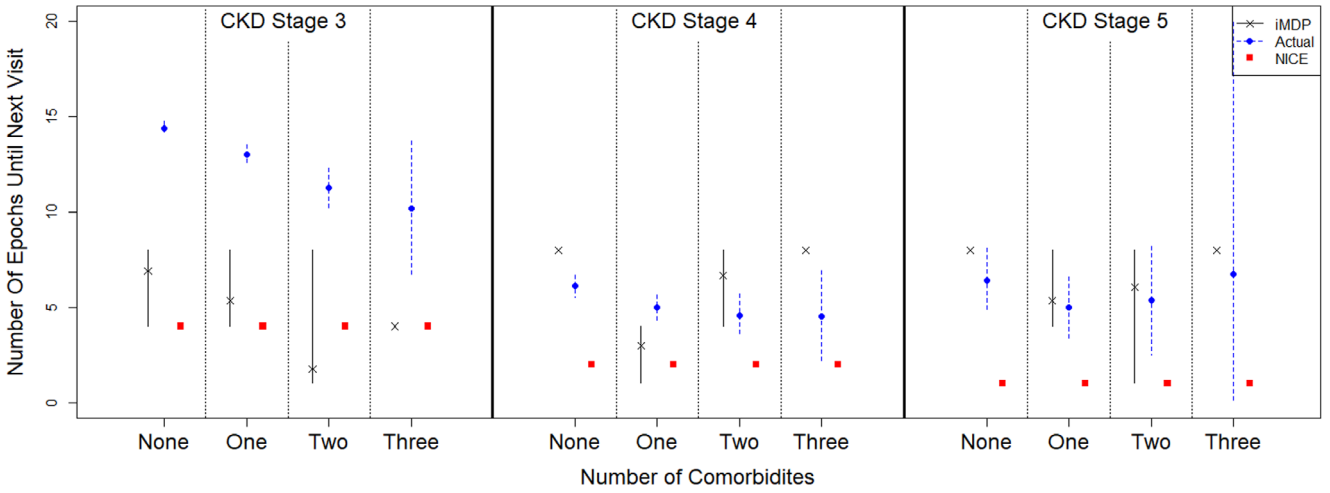
The appointment hardships experienced by most veterans are associated with the distance and time required to travel and attend an appointment (Buzza et al. 2011). It should be noted that NICE is based in England, which in 2008 became the most densely

Table 6 iMDP Recommended Follow-up Policies (i) for Different Patient Health States

Kidney disease		Stage 3	Stage 4	Stage 5
dhv	000	12 (age 60–80); 6 (age 81–90)	12	12
	001	12	6	6
	010	6	1.5	12
	011	3	12	12
	100	6	6	6
	101	3	6	12
	110	1.5	12	6 (age 60–63); 1.5 (age 64–90)
	111	6	12	12

Note: *dist* = 89 miles.

Figure 5 Comorbidity Count Effect [Color figure can be viewed at wileyonlinelibrary.com]



populated country in Europe (Khan 2008) at 395 individuals per square kilometer. In the same year, the population density in the United States was 33.24 per square kilometer. The differences between the two countries could suggest a significant discrepancy in their average distance travelled to an appointment. This highlights the importance of developing guidelines specifically designed for monitoring rural patients and explains the increased interest and recent investments in telehealth options for monitoring CKD in the VA healthcare system (Crowley et al. 2017).

Observation 4 (Impact of Past Research). *The iMDP appointment schedules for patients in CKD Stage 5 are most comparable to the actual policies employed by VA nephrologists.*

In Figure 5, the appointment frequencies of the Actual and iMDP settings for CKD Stage 5 overlap across all comorbidity groups. The similarities between the mean iMDP and the mean actual appointment policies may be due to the extensive efforts devoted to improving the care of patients near dialysis, as discussed in section 2.

Observation 5 (Benefit vs. Burden). *There exists a nonlinear relationship between patients' comorbidity count and iMDP appointment frequencies.*

For CKD Stages 4 and 5, the average iMDP appointment frequency increases the most when a patient develops his first comorbidity (i.e., transitions from zero to one comorbidity). The biggest drop for CKD Stage 3 is observed when a patient develops his second comorbidity (i.e., transitions from one to two comorbidities). This health status change can be viewed as a shock to relatively mobile patients and thus frequently seeing a doctor in person is still perceived as beneficial despite the patients' appointment disutilities. This is because CKD Stage 3 patients are healthier and thus have a higher tolerance for frequent visits even in the presence of more complex comorbid conditions. On the other hand, for all CKD Stages, the average iMDP appointment frequency decreases when a patient develops a third comorbidity. This is primarily due to the mobility challenges and the decrease in the marginal benefit of face-to-face interaction with the nephrologist. For such complex patients, it might be more beneficial to slowly substitute (1) maintenance kidney care with palliative care and (2) in-person with telemedicine appointments. Increasing appointment frequencies may no longer benefit the patient due to his high health state disutilities and proximity to a terminal state (dialysis and/or death).

5.2. iMDP Evaluation

To assess the iMDP performance, we compare it with the NICE guidelines and the actual nephrologist visit schedules. Ideally, we would design a cohort study in which patients are randomized in two groups. The control group will follow a schedule set by a nephrologist, while the case group will follow the iMDP schedule in Table 6. To avoid provider bias, both groups would be seen by the same nephrologists to form a set of matched pairs. To contrast these two scheduling policies, the study would need to monitor patients for an extended period of time, due to the long-life expectancies of some patient groups (O'Hare et al. 2012). This is a very challenging task, requiring various bureaucratic approval procedures, and is a part of our future research plan with the hospital system under

study. For now, we will conduct numerical studies to validate our model and gain insights.

5.2.1. iMDP vs. NICE Schedules.

OBSERVATION 6. (iMDP vs NICE). *The iMDP outperforms the NICE guidelines across the entire state space.*

To quantify the QALD performance difference (in %) between the iMDP and NICE policies, we use the age-averaged QALDs: $\left\{\sum_{age=60}^{90} \frac{v_n^{iMDP}(\mathbf{s}) - v_n^{NICE}(\mathbf{s})}{v_n^{NICE}(\mathbf{s})} * 100\right\} / \{90-60+1\}$. v_n^{iMDP} is the outcome of the iMDP policy; while v_n^{NICE} is that from the NICE guidelines; both can be derived by Equation (1). Recall that an epoch is 1.5 months; and NICE recommends Stage 3 patients to visit doctors every six months (4 epochs); Stage 4 patients every three months (2 epochs); and Stage 5 patients every 1.5 months (1 epoch), regardless of age, comorbidities, and distance to a nephrologist.

To understand how each component of the iMDP state space impacts CKD patient's QALD, we analyzed different scenarios (see Table 7) by including all possible state space comorbidity and age/no age combinations. Namely, we examine all on/off combinations for each element of (*d*, *h*, *v*, *age*), which translates into 2 * 2 * 2 * 2 = 16 scenarios. We compared the NICE policy with the iMDPs result for each of the 16 scenarios. Furthermore, for each setting we compared the two policies across different distance-to-nephrologist measures, with min and max distance ranging from 1 to 200 miles (Buzza et al. 2011). We found that the iMDP outperformed the NICE policy across all examined state space settings, with the improvement ranging from 0.34% to 76.38%.

The regression model in Table 8 details the contribution of each iMDP state space component. The dependent variable is the percentage improvement in QALD over NICE when the iMDP is applied. The predictors include patients' CKD Stage (CKD Stage 3 is the baseline category), the number of comorbidities incorporated into the iMDP (0 comorbidities is the baseline category), whether age is accounted for by the iMDP (Yes = 1; No = 0), and the distance to a nephrologist (ranging from 1 to 200 miles). We find that the regression model has an R-sq of 0.89, and all iMDP state space components are important and significantly boost the iMDP performance over that of the NICE policy.

OBSERVATION 6A (iMDP vs NICE). *Comorbidities are the most significant contributors to the iMDP dominance followed by the Age and Distance measures.*

When incorporating only one comorbidity into the iMDP model, we find that the iMDP outperforms NICE with an improvement ranging from 0.46% (CKD Stage 3) to 7.84% (= 0.46 + 7.38—CKD Stage 5). When two comorbidities are included the dominance ranges from 1.27% to 10.19%. Finally, for three comorbidities, the dominance is between 3.88% and 9.68%. The iMDP also benefits from incorporating patient's age into its state space, with an additional 0.72% contribution. Finally, incorporating the distance measure has an impact which surpasses the importance of age for some rural patients. For example, when a patient lives 200 miles from his nephrologist, the iMDP outperforms NICE by 0.0410% ($= 0.0049 * 200 - 0.00002 * 200^2$), 0.2687% ($= (0.0049 + 0.0011) * 200 - 0.00002 * 200^2$) and 0.9396% ($= (0.0049 + 0.0045) * 200 - 0.00002 * 200^2$) for patients in CKD Stages 3, 4, and 5, respectively. To better understand what the distance-based % improvement entails, we examined the raw data and found the average number of days gained

Table 7 iMDP State Space Combinations Examined

State space	Comorbidities	CKD (k)	Diabetes (d)	Heart failure (h)	Vascular disease (v)	Age
$\mathbf{s} = (k)$	0	×				
$\mathbf{s} = (k, age)$	1	×				×
$\mathbf{s} = (k, d)$	1	×	×			
$\mathbf{s} = (k, d, age)$	1	×	×			×
$\mathbf{s} = (k, h)$	1	×		×		
$\mathbf{s} = (k, h, age)$	1	×		×		×
$\mathbf{s} = (k, v)$	1	×			×	
$\mathbf{s} = (k, v, age)$	1	×			×	×
$\mathbf{s} = (k, d, h)$	2	×	×	×		
$\mathbf{s} = (k, d, h, age)$	2	×	×	×		×
$\mathbf{s} = (k, d, v)$	2	×	×		×	
$\mathbf{s} = (k, d, v, age)$	2	×	×		×	×
$\mathbf{s} = (k, h, v)$	2	×		×	×	
$\mathbf{s} = (k, h, v, age)$	2	×		×	×	×
$\mathbf{s} = (k, d, h, v)$	3	×	×	×	×	
$\mathbf{s} = (k, d, h, v, age)$	3	×	×	×	×	×

Note: $dist \in [1,200]$ is considered in all 16 scenarios above.

Table 8 Percentage Improvement of iMDP over NICE

Variables	Coefficient (s.e.)	*p*-value
(Intercept)	−0.5112 (0.1092)	0.0000
CKD Stage 4	10.0235 (0.1315)	0.0000
CKD Stage 5	38.5478 (0.1315)	0.0000
No. Comorbidities = 1	0.4621 (0.0953)	0.0000
No. Comorbidities = 2	1.2677 (0.0918)	0.0000
No. Comorbidities = 3	3.8828 (0.0935)	0.0000
Distance	0.0049 (0.0007)	0.0000
sq-Distance	−0.00002 (0.0000)	0.0000
Age Included = Yes	0.7174 (0.0546)	0.0000
CKD Stage 4 * No. Comorbidities = 1	3.9073 (0.1347)	0.0000
CKD Stage 5 * No. Comorbidities = 1	7.3758 (0.1347)	0.0000
CKD Stage 4 * No. Comorbidities = 2	5.7046 (0.1298)	0.0000
CKD Stage 5 * No. Comorbidities = 2	8.9307 (0.1298)	0.0000
CKD Stage 4 * No. Comorbidities = 3	5.7924 (0.1323)	0.0000
CKD Stage 5 * No. Comorbidities = 3	4.8884 (0.1323)	0.0000
CKD Stage 4 * Distance	0.0011 (0.0004)	0.0062
CKD Stage 5 * Distance	0.0045 (0.0004)	0.0000

across all distance measures for patients with CKD Stages 3/4/5 were 8.14/17.60/75.02 days.

Observation 6B (iMDP vs NICE). *The iMDP superiority is more evident among sicker patients.*

The dominance of the iMDP over NICE is more pronounced for sicker patients. This is marked by the large coefficients in CKD Stages 4 and 5: 10.02 and 38.55, respectively. This dominance is magnified for patients with one or more comorbidities. These conclusions are supported by the results in Table 8, where (1) advanced CKD Stages, (2) high comorbidity counts and (3) the interaction terms between patient's CKD Stage and comorbidity count all have large coefficients.

Observation 6C (iMDP vs NICE). *There exists a non-linear relationship between the iMDP dominance and patient's proximity to a nephrologist.*

Figure 6 compares the difference in QALD performance between the NICE model and the iMDP by considering patient's CKD Stage and distance to a nephrologist. It shows how the improvement differs for patients living close or far away from their nephrologist (see x-axis where distance varies from 1 to 200 miles). Note that, we have included gaps in the y-axis of the figure (between 0.5 and 10.00 and between 10.50 and 38.5) to highlight the curve in the three lines. It shows that the iMDP provides greater benefits for patients in more advanced CKD Stages. Additionally, the dominance of the iMDP over the NICE policies depends on the distance a patient needs to travel to attend a doctor's appointment and his CKD Stage. Incorporating the distance information when making follow-up appointment decisions could enhance patient's QALD significantly.

5.2.2. iMDP vs. Actual Schedules. Figures 7 and 8 illustrate the differences between the iMDP recommendations and current VA practices. Each graph pertains to a single individual, and contains his eGFR laboratory results, comorbidity onset, actual nephrology appointments, and iMDP recommended schedules. To determine a patient's CKD Stage, we use his most recent eGFR reading. Namely, eGFR between 30 and 60 mL/min/1.73m^2 corresponds to CKD Stage 3; eGFR between 15 and 30 corresponds to Stage 4; while eGFR below 15 corresponds to Stage 5. The tick marks on the x-axis of both graphs indicate the beginning of each year we have information on, that is, 2012 is a shorthand for 01/01/2012.

Observation 7 (Continuity of Care). *The iMDP is not overly demanding but ensures that each patient is seen at least once a year, which is not currently enforced by the VA.*

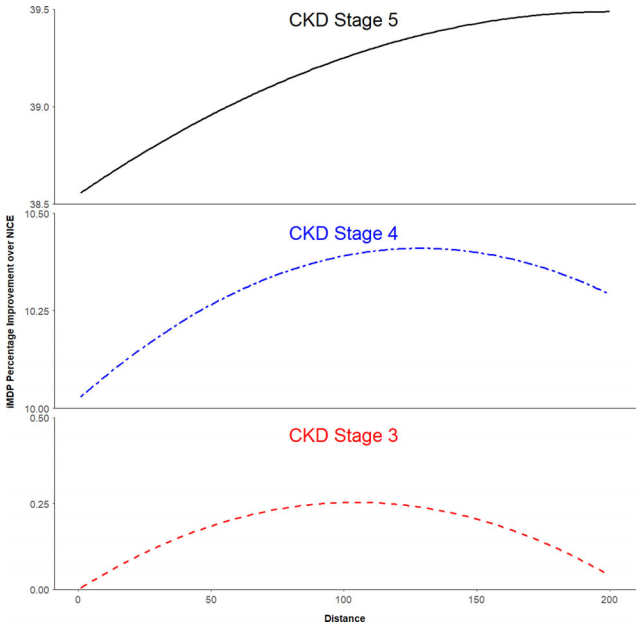
Our model optimizes a patient's QALD. Depending on the patient's health state, the iMDP may recommend more or fewer appointments than the ones attended by past patients. Figure 7 shows the iMDP recommends four more visits than the ones actually attended, while Figure 8 suggests the same number of visits as the one attended by the patient. Note that, the iMDP ensures that the patient is seen at least once a year, which is not enforced by the VA as evidenced by the large gaps between actual appointments in Figure 7.

In Figure 7, the Stage 5 senior patient visited a nephrologist frequently after his first comorbidity onset (vascular disease on 05/23/2011) even though his eGFR was stable. He experienced a significant eGFR deterioration in 2013 but was never seen by a nephrologist. In contrast, following the vascular disease diagnosis the iMDP recommends a visit every 6 months between 2011 and 2014. In hindsight, a single appointment in 2011 would have been appropriate as the patient stayed relatively stable in this time period. Additionally, having multiple appointments in 2012 and 2013 would have benefited the patient as he substantially deteriorated in that time period and these visits might have stabilized his kidney disease progression, diabetes and heart failure onsets.

Observation 8 (Stability). *Continuous and approximately equally spaced appointments (consistent with NICE guidelines) may fail to stabilize disease progression.*

In Figure 8, the Stage 4 patient with heart failure was first seen at the age of 66. His health deteriorated over time, as he was subsequently diagnosed with

Figure 6 **iMDP vs. NICE—Accounting for Distance and Chronic Kidney Disease Stage [Color figure can be viewed at wileyonlinelibrary.com]**



vascular disease and diabetes. Unlike the patient in Figure 7, he was continuously monitored by a nephrologist, evident in the frequent and approximately equispaced visits. We believe that the iMDP model would have benefited the patient as it suggests more frequent clinic visits in his early stages of disease progression, which are spaced out as his health deteriorates because he will incur higher visit disabilities and the appointment benefit will be outweighed by the burden.

5.3. Model Validity

To better understand the validity of the iMDP model we first perform an endogeneity check. Subsequently, we conduct sensitivity analyses to understand how changes in parameters impact our model outcomes.

5.3.1. Endogeneity Check. The MDP model is parameterized using data from (1) published research—to estimate the *immediate rewards*; (2) a survival analysis model—to predict the *terminal reward*; and (3) a CBR model—to estimate the *transition probability*. As the *immediate rewards* are from the literature, we cannot perform endogeneity checks on these estimates. The second set of parameters is from our survival analysis model, which utilizes censored data to predicts patient's time until event (dialysis or death). The goal is to provide an accurate forecast, not to determine causality. The CBR model is also a prediction model, which is used to identify the nearest neighbors (similar patients) and then estimate the iMDP transition probability matrices. As both the survival and the CBR models fall under the umbrella of prediction techniques, not what-if analysis or hypothesis testing, endogeneity is not a major concern (Tang 2019).

The standard OLS methods require independent variables (x's) to be uncorrelated with the error term in the model. If a predictor (z) is correlated with the model error terms, then endogeneity exists. As noted above endogeneity is not a major concern for the CBR model. Nevertheless, we perform endogeneity tests to provide further check by fitting a model, with eGFR as the dependent variable (determining patient's CKD Stage) during an appointment using our CBR data (patient's health status). The current eGFR is a function of patient's health state (x's include age,

Figure 7 **Patient #1 Actual vs. iMDP Appointments: Chronic Kidney Disease Stage 5 and 82 Years Old in 2011 [Color figure can be viewed at wileyonlinelibrary.com]**

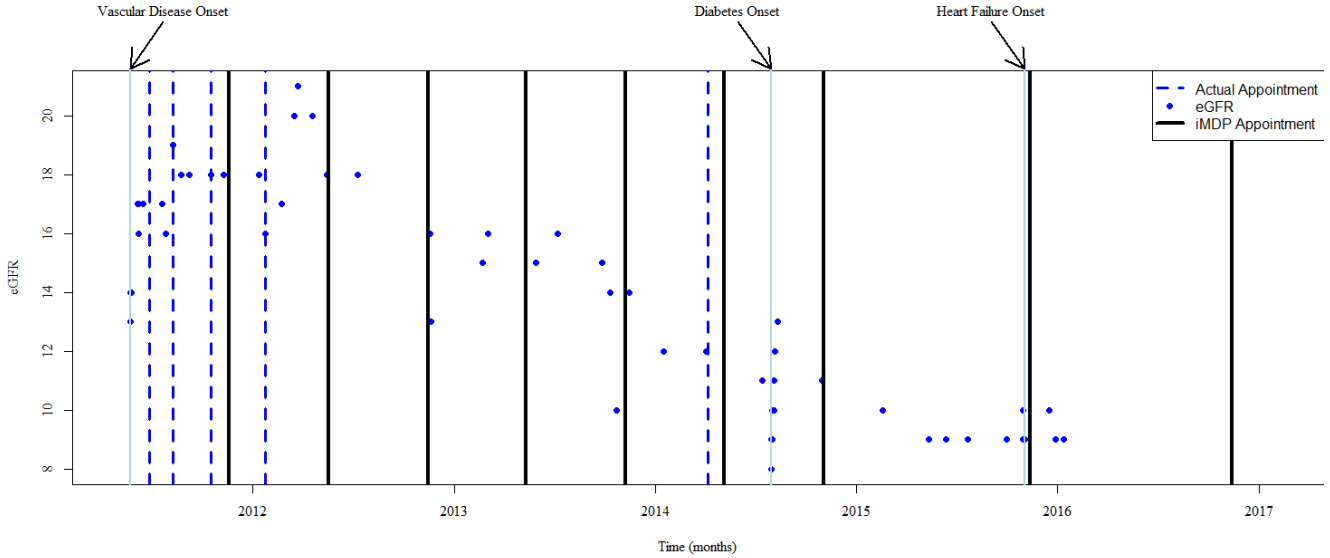
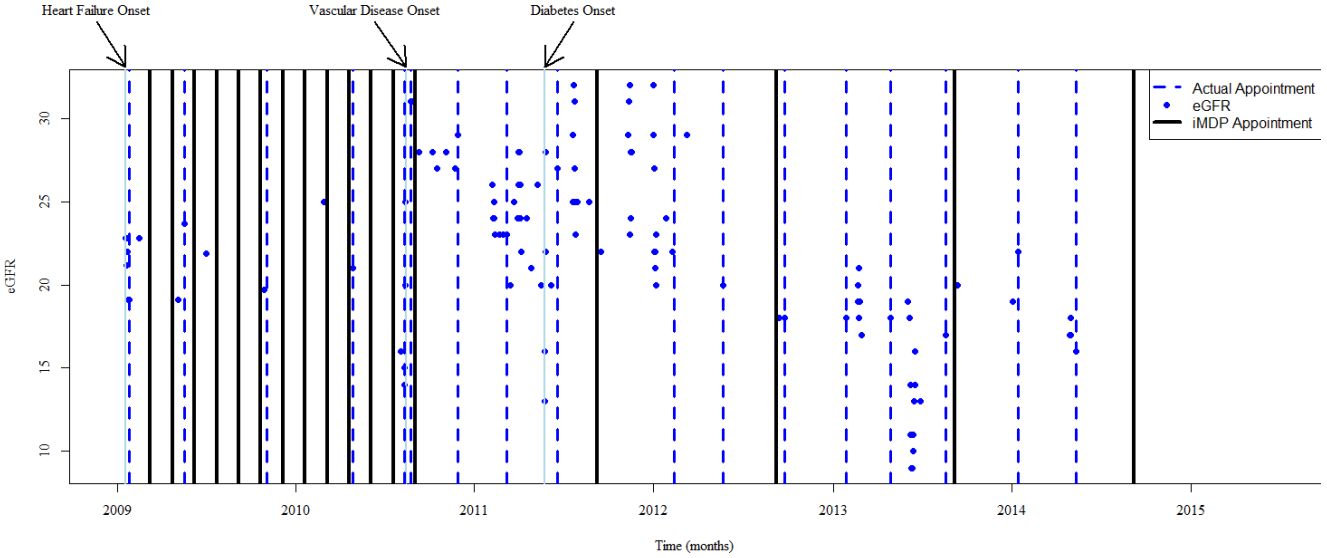


Figure 8 Patient # 3 Actual vs. iMDP Appointments: Chronic Kidney Disease Stage 4 and 66 Years Old in 2009 [Color figure can be viewed at wileyonlinelibrary.com]



diabetes, heart failure, vascular disease, and CKD status) during his last nephrology visit and the time (in days) since his last nephrology visit (z). To perform our endogeneity test with respect to the time (in days) since last nephrology visit, we run three models (OLS, two-step least squares, and an instrument variable model) and give results in Table 9. Only the IV model can be used to test for endogeneity. As the results of all the three models are comparable, we believe all three model outcomes are reliable. Besides the predictors listed in the IV model in Table 9, we also include instrumental variables (Hospital ID, systolic blood pressure and nephrology visits in the 12 months prior to the previous appointment—information utilized by the CBR model). From the weak instruments test, we find that not all instruments in the IV model are weak ($p < 0.0001$). Also, from the (Wu-)Hausman test we find that no significant endogeneity is observed ($p = 0.8940$). These observations further alleviate our endogeneity concerns.

5.3.2. Sensitivity Analysis. To better understand the validity of the iMDP model, we perform sensitivity analysis, which also help us to examine the stability of our numerical results. More specifically, we examine how the optimal appointment policy for a given health state **s** changes when we perturb (1) *dist*, (2) N and $\mathbf{P_i}$, and (3) at_{appt} and wt_{appt}.

Observation 9 (Distance Sensitivity Analysis). *The iMDP policies differ between the rural and urban patients.*

The iMDP policies reported in Table 6 are obtained for $dist = 89$ miles. We examine the impact of distance on the iMDP policies, where $dist \in \{1,200\}$ (Buzza et al. 2011). We observe that the optimal appointment frequencies remain stable for rural individuals (living 16 or more miles away from their nephrologist). However, for urban veterans (living no more than 15 miles away from a nephrologist) the policy differs from the results in Table 6, and patients are recommended to visit a nephrologist more frequently as travelling is not a serious burden. The discrepancy highlights the importance of considering the proximity of patients to their physicians. Note that distance is not considered by NICE, as it was developed in one of the most densely populated countries in Europe—England.

Observation 10 (**s**, N and $\mathbf{P_i}$ Sensitivity Analysis). *Results remain stable across all patient states* (**s**), *regardless of the planning horizon* (N) *and transition probability* ($\mathbf{P_i}$), *that is, the model is robust.*

Our results remain stable in over 90% of perturbed cases across all planning horizons and states. The model always suggests the least demanding and the most beneficial action to minimize disease progression. This could explain why in settings where a patient is very likely to progress (i.e., the progression probability is at least 90%) the model suggests spacing out appointments as their benefit will outweigh the burden on the patient. Please refer to Appendix B for details.

Observation 11 (Appointment Settings Sensitivity Analysis). *In general, the iMDP outcomes remain robust to perturbations in the appointment wait-time* (wt_{appt}) *and length* (at_{appt}). *However, certain patients may be sensitive to the changes in* wt_{appt} *and* at_{appt}.

We examine how sensitive our results (i.e., appointment schedule, i) are to changes in the appointment wait-time and length. We record the optimal appointment policies for patients living 89 miles away from a doctor (Buzza et al. 2011). We evaluate the waiting time (wt_{appt}) between 0 and 6 hours in increment of 1 minute, based on the nephrologist's typical work schedule (Williams 2018). We also set the appointment length (at_{appt}) between 5 minutes and 2 hours in increment of one minute, as we do not expect a specialist's appointment to last <5 minute and more than 2 hours. We observe that the parameter perturbations affected the appointment policies in only 0.3307% of all the policies. Still, some patient classes are sensitive to changes in the two parameters.

We highlight two of the patient classes where the appointment frequency changes are noticeable. In Figure 9, (1) to the left is the result for a 90-year-old patient with CKD Stage 3 and vascular disease $\mathbf{s} = (3, 0, 0, 1, 90)$, while (2) to the right is the result for a 64-year-old patient with CKD Stage 5, diabetes, and heart failure $\mathbf{s} = (5, 1, 1, 0,64)$. The graphs' widths span the appointment lengths (the time being examined, at_{appt}, ranges from 5 to 120 minutes). The parameter across the graph lengths is the waiting time (wt_{appt}). Note that, the left graph's waiting time starts at 0 minutes, while the right graph starts at 83 minutes. The reason why the graphs have been cropped is because of their length. Also, all cropped regions are the same as the ones at the edges of the graph. For example, if the CKD Stage 3 patient's waiting time exceeds 70 minutes he is recommended for an annual checkup ($i = 8$, 12 months). Similarly, if the CKD Stage 5 patient's waiting time is less than (exceeded) 83 (200) minutes he is recommended a follow-up in 1.5 (6) months. The optimal policies for each shaded region are presented in bold in the upper left corner for the red regions and lower right corner for the blue regions.

Based on the left graph in Figure 9, we find that older and healthier patients, for example, $\mathbf{s} = (3, 0, 0, 1, 90)$, will tolerate more frequent visits ($i = 4$ vs. $i = 8$) under certain waiting time ($wt_{appt} < 70$ minutes) and appointment length ($at_{appt} < 72$ minutes) conditions. However, for CKD Stage 3 patients with vascular disease who are younger than 90, the iMDP would recommend annual checkups regardless of wt_{appt} and at_{appt}. Additionally, we see a higher tolerance for appointment lengths than wait times in the $\mathbf{s} = (3, 0, 0, 1, 90)$ patients (i.e., max. $wt_{appt} = 70$ minutes vs. max. $at_{appt} = 72$ minutes). Finally, the right graph in Figure 9 shows that sicker patients, for example, $\mathbf{s} = (5, 1, 1, 0, 64)$, are more tolerant of longer wait-times. For example, when the waiting time is very long (up to 200 minutes) the CKD Stage 5 patient is still advised to attend frequent visits ($i = 1$, 1.5 months), while the CKD Stage 3 patient visit frequency is reduced (from 6 months to 12 months) when the waiting time exceeds 70 minutes.

Table 9 eGFR Equation: OLS, 2SLS, and IV Models Compared

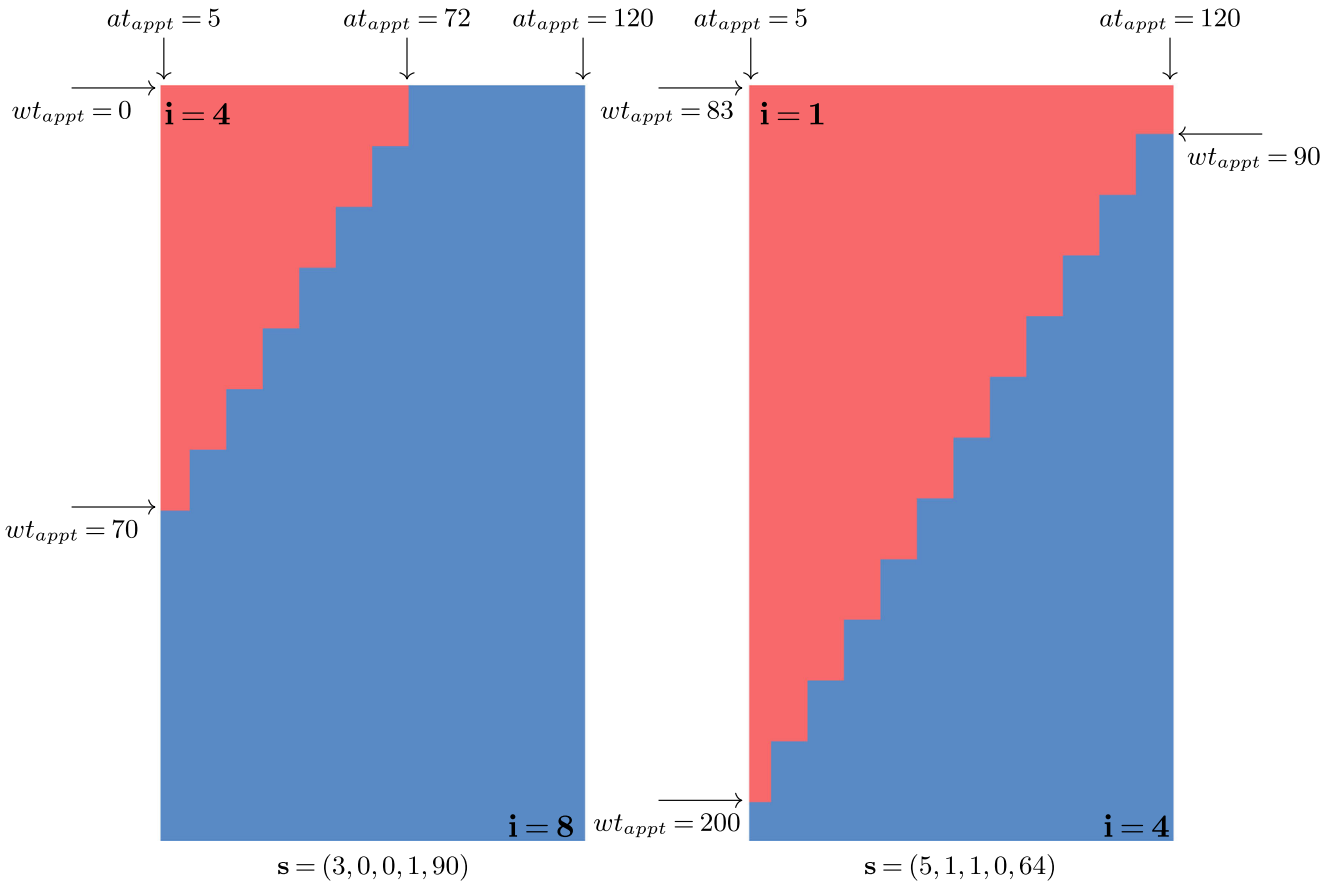
	Dependent variable: eGFR		
	OLS	explicit 2SLS	IV
Constant	43.3759	43.3667	43.3667
	(0.1218)	(0.1404)	(0.1400)
Time Since Last Appointment (in days)	−0.0025		−0.0025
	(0.0001)		(0.0003)
E[Time Since Last Appointment (in days)]		−0.0025	
		(0.0003)	
Age	−0.0228	−0.0227	−0.0227
	(0.0017)	(0.0017)	(0.0017)
Diabetes	−0.0202	−0.0195	−0.0195
	(0.0368)	(0.0373)	(0.0372)
Vascular Disease	−0.5326	−0.5328	−0.5328
	(0.0374)	(0.0376)	(0.0374)
Heart Failure	−0.8543	−0.8545	−0.8545
	(0.0632)	(0.0634)	(0.0632)
CKD Stage 4	−18.9919	−18.9894	−18.9894
	(0.0385)	(0.0432)	(0.0430)
CKD Stage 5	−30.3185	−30.3165	−30.3165
	(0.0530)	(0.0553)	(0.0552)
Observations	182,942	182,942	182,942

6. Conclusion

Chronic conditions such as CKD, heart failure, cancer, and diabetes are among the most common, expensive to treat, and preventable diseases. According to the CDC, 7 of the top 10 causes of death in the United States are contributed to chronic conditions. The CDC has also reported that 117 million Americans have at least one chronic condition, which could explain why 86% of the money spent on healthcare ($2.7 trillion per year) are associated with treating chronic and mental diseases. This enormous economic burden can be reduced if doctors offer more rigorous treatments plans.

In this research, we propose a tool for improving the care of CKD patients. It represents a valuable addition to the literature as being the first study using the MDP-based approach to effectively schedule appointments for chronically ill patients. Using the **R Shiny** library, we can build a user-friendly app. It can prompt the iMDP-based follow-up appointment timing when the health status of a CKD patient is entered. Such a tool can help nephrologists when scheduling their patients' next visit. The proposed iMDP framework ensures that every patient would follow a well-timed doctor visit plan. We find that our data-driven policy significantly outperforms the NICE guideline, which does not account for

Figure 9 Sensitivity Analysis—Sample Results [Color figure can be viewed at wileyonlinelibrary.com]



patient age and existing comorbidities. The iMDP ensures that patients are seen by a nephrologist at least once a year, which is not currently enforced by the VA.

Past research has mainly focused on CKD Stage 5 patients. Upon examining patients in CKD Stage 5 we find no significant difference between the iMDP optimal policy and decisions made by VA nephrologists. Our observation suggests that past research has helped improve the care for the sickest patients. Unfortunately, there exists a significant discrepancy between iMDP and VA practices for patients in CKD Stages 3 and 4. For example, the iMDP suggests a significant increase in CKD Stage 3 patients' appointment frequencies.

Our iMDP results are in agreement with (1) Gijsen et al. (2001), who found that comorbidities and health care utilization are related, and (2) O'Hare et al. (2007), who suggest that for CKD Stage 3–5 patients, age impacts disease progression in some patient categories and should be considered when designing CKD-management strategies. For patients near kidney failure and/or death, the iMDP suggests fewer monitoring appointments. This policy is sensible to individuals in CKD Stage 5 with multiple comorbidities, as they are often faced with the option of conservative (palliative) or active (dialysis) treatment (Fassett et al. 2011). If conservative treatment is chosen, regular monitoring appointments will be largely substituted by interactions with a palliative care team. If dialysis is initiated, the patient will begin attending a dialysis clinic, which is beyond the scope of this study. We should note that the iMDP suggests significant changes in the appointment frequency for CKD patients. Before our policies are implemented, hospitals need to determine if they have enough nephrologists on staff to accommodate them, which will allow for a smooth transition and better patient and provider satisfaction.

The chronic disease used to validate our framework produces results with important demand-for-care implications and reasonable scheduling policies. Still, our research has its limitations, as it is based on a cohort of VA patients with low gender diversity and missing race information, which prohibit us from incorporating gender and race in our state space. Therefore, our results should be used with caution when optimizing the appointment frequencies of

patients underrepresented in the data set. This is particularly important for African Americans with CKD, as they often experience faster disease progression (Hsu et al. 2003).

Our work has provided an important insight into the optimal monitoring strategies for patients with CKD. Several research directions remain to be explored. First, as our model focuses on nephrology appointments, it cannot be used to suggest other appointments (i.e., with a cardiologist, endocrinologist, nephrologist, PCP) that could benefit a CKD patient. To address this drawback, we plan on enhancing the model so that it can specify the optimal timing and type of follow-up appointments, where appointment types would include nephrology, cardiology, endocrinology, primary care, etc. Stratifying across specialties would make our MDP even more useful for hospital management. Second, to generalize our approach and offer a generic model for other types of chronic diseases, we will relax the appointment constraint in future research. Namely, we will treat the time between visits as a continuous variable and allow the model to schedule the next appointment any time over a longer planning horizon. Third, rather that restricting ourselves to patients between the ages of 60 and 90, we can consider individuals from all ages and cluster them to reduce our state space dimensionality. Fourth, it will be beneficial to examine theoretical results and identify the conditions under which our numerical and theoretical findings will be fully aligned. Finally, to help facilitate the implementation of the iMDP monitoring approach, a study needs to identify the staffing levels needed to support the iMDP driven demand change.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix A: iMDP Literature Review Components.
Appendix B: Sensitivity Analysis.