Treatment practices of patients with advanced kidney disease in the US Department of Veterans Affairs, 2000-2011

Susan Pamela Yi Wong

A thesis
submitted in partial fulfillment of the
requirements for the degree of

Master of Science

University of Washington
2017

Committee:

Annette Fitzpatrick
Paul Hebert
Ann O'Hare

Program Authorized to Offer Degree:

Epidemiology, School of Public Health

University of Washington

Abstract

Treatment practices of patients with advanced kidney disease in the US Department of Veterans Affairs, 2000-2011

Susan Pamela Yi Wong

Chair of Supervisory Committee:
Professor Annette L. Fitzpatrick
Department of Epidemiology
Associate Dean
School of Public Health

It is not known what proportion of US patients with advanced chronic kidney disease (CKD) receive renal replacement therapy (RRT) with maintenance dialysis or kidney transplant. In other developed countries, receipt of RRT is highly age-dependent and is the exception rather than the rule at older ages. We conducted a retrospective study of a national cohort of 28,568 adults who were receiving care within the Department of Veterans Affairs (VA) and had very advanced CKD (i.e., a sustained estimated glomerular filtration rate <15 ml/min/1.73m^2) between January 1, 2000 to December 31, 2009 to determine how often patients with advanced CKD do not receive RRT, the characteristics of these patients and the clinical context in which these decisions occur.

We used linked administrative data from the US Renal Data System (US national registry of RRT or USRDS), VA and Medicare to identify cohort members who received RRT

during follow-up through October 1, 2011 (n=19,165). Of the 9,403 patients who did not receive RRT, we performed an in-depth review of VA-wide electronic medical records for a 25% randomly selected sample (n=2,252) to determine the treatment status of their CKD. We used inductive and deductive approaches for content analysis to complete medical record review. Initially, two nephrologists (S.P.Y.W. and A.M.O.) reviewed the progress notes of 200 randomly selected patients in the sample to identify clinically distinct groups with respect to the decision for dialysis to treat their advanced CKD (ie., received dialysis, discussing and/or preparing for dialysis, and decision against dialysis). The remaining 2,052 patients in the sample were assigned to a pre-specified treatment group. The results of chart review were used to estimate the proportion and 95% confidence interval (CI) of the overall cohort expected to belong to each treatment group and the estimated distribution of treatment groups within each age group. We then identified patients with an administrative record of having received RRT during follow-up based on USRDS enrollment or dialysis procedure codes and assigned them as the referent group in between-group comparisons of socio-demographic and clinical characteristics. We assessed the characteristics associated with membership in each treatment group using a multinomial logistic regression model adjusted for all baseline patient characteristics and calendar year of cohort entry. Sensitivity analyses were conducted in which models were developed after stratification by tertile of Gagne comorbidity score to evaluate for differences in treatment practices based on burden of comorbidity.

Overall, two-thirds (67.1%) of cohort members received RRT based on linked administrative data. Results of the chart review determined that an additional 7.5% (95% CI 7.2-7.8) of cohort members had in fact received dialysis that was not captured in USRDS or administrative data, 10.9% (95% CI 10.6-11.3) were preparing for and/or discussing dialysis but had not started dialysis at most recent follow-up, and in 14.5% (95% CI 14.1-14.9), a decision had been made by the patients themselves, their family members and/or healthcare provider not to pursue dialysis. Compared with the referent group, patients in whom a decision against dialysis had been made were older, more often white, had a higher burden of comorbidity and had less nephrology care in the year prior to cohort entry. The percentage of cohort members who received or were preparing to receive RRT ranged from 96.2% (95% CI 94.4-97.4) for those <45 years to 53.3% (95% CI 50.7-55.9) for those aged ≥85 years. Results were similar after stratification by comorbidity score. In conclusion, in this large US cohort of patients with advanced CKD, the majority received or were preparing to receive RRT. This was true even among the oldest patients with the highest burden of comorbidity.

Introduction

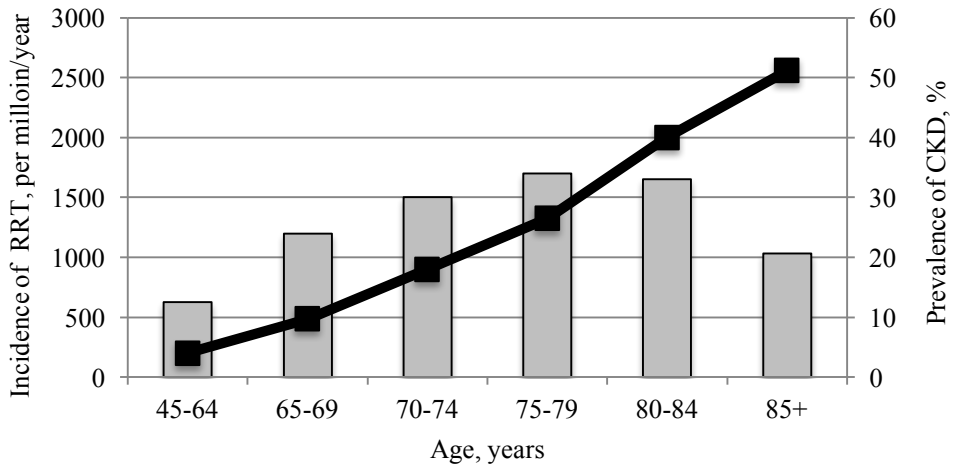
Currently, there are over 661,000 Americans receiving renal replacement therapy (RRT), including maintenance dialysis and kidney transplant, for their advanced chronic kidney disease (CKD).[1] Medicare is the primary payor of RRT, which accounts for 7.1% ($30.9 billion) of overall Medicare paid claims.[1] The incidence of RRT in the US is 363 cases/million/year and is several fold higher than in European nations.[1,2] Whether the relatively higher incidence of RRT in the US reflects a greater burden of kidney disease in the source population or differences in treatment practices for RRT is not known.

Most data on the course of advanced CKD in the US come from the national registry of RRT, the United States Renal Data System (USRDS). The USRDS is a comprehensive national data system that collects, analyzes, and distributes information about patients who receive RRT in the United States. The USRDS is funded by the National Institute of Diabetes and Digestive and Kidney Diseases and collaborates with the Centers for Medicare & Medicaid Services (CMS) to prospectively gather demographic and clinical information on all US patients treated with chronic dialysis and kidney transplant. As mandated by the CMS, patients are enrolled in the USRDS registry soon after initiation of RRT. Information on patients is collected using standardized forms (CMS-2728 form) completed by the nephrologist around the time of initiation of RRT.

However, similar to many other national registries of RRT, the USRDS does not collect information on patients who reach the advanced stages of CKD but are not treated with RRT. There are several lines of indirect evidence to suggest that there may be a large potential “reservoir” of patients with advanced CKD in this country who are not

treated with RRT, especially at older ages (>75 years). While the prevalence of CKD increases linearly with age, the incidence of RRT as reported by USRDS plateaus and

Figure 1. Age differences in prevalence of CKD (black line) and incidence of RRT (grey bars) in the US



Abbreviations: CKD, chronic kidney disease; RRT, renal replacement therapy
References 1,3,5,31 include the original data.

then declines at older ages (Figure 1).[1,3-7] Several studies outside the US suggest that it is relatively common for patients with advanced CKD not to receive RRT, especially at older ages.[8,9] For instance, prior studies conducted in Canada[8] and Australia and New Zealand[9] using RRT registry and administrative data indicate that approximately half of patients with advanced CKD do not receive RRT. However, there is marked international variation in use of RRT,[1,2,6] making it uncertain whether the results of these studies are generalizable to the US. Source data for these studies also lacked information on the circumstances leading to patients not receiving RRT, such as whether there had been a decision not to offer or receive RRT.

The Department of Veterans Affairs (VA) is the largest integrated healthcare system in the US, and serves 8.8 million veterans each year. The VA is a healthcare organization that provides clinical care through a network of over 1,700 facilities around the country as well as serves as a payor for healthcare for veterans who receive care at non-VA facilities. We conducted a retrospective study among a national cohort of patients receiving care within the VA to determine how often patients with advanced CKD do not receive RRT, the characteristics of these patients and the clinical context in which these decisions occur.

Methods

Data Sources

We constructed the analytic dataset by linking the following data sources: VA Vital Status (which contains Veteran's demographic information), VA MedSAS (which contains information on care received within the VA), VA Fee Basis (which contains information on care received in non-VA facilities but paid for by the VA), Medicare Institutional and Physician Supplier, and USRDS files.

Study Population

Using VA clinical and administrative data sources, we identified all veterans aged ≥18 years with advanced CKD. Advanced CKD was defined in accordance with the Kidney Disease Outcomes Quality Improvement (KDOQI) clinical practice guidelines for CKD as having an estimated glomerular filtration rate (eGFR) <15 ml/min/1.73m^2 on at least two outpatient tests drawn at least 90 days apart between January 1, 2000 and

December 31, 2009 (N=50,121).[10] Date of cohort entry was defined as the date of the second eGFR <15 ml/min/1.73m^2. We excluded patients who received RRT prior to cohort entry using two strategies. First, patients who received RRT were identified based on registration in USRDS using linked USRDS records (n=20,537). Second, we performed a procedure code search for dialysis in patients' linked Medicare claims and VA inpatient and outpatient treatment and Fee Basis files (which captures care received at non-VA facilities but that is paid for by the VA) on or before the date of cohort entry (n=1,016). This yielded an analytic cohort of 28,568 patients. Patients were followed through date of death (obtained from the VA Vital Status File) or October 1, 2011.

The Institutional Review Boards at the Seattle VA Puget Sound Healthcare System and the University of Washington approved this study and waived the requirement to obtain informed consent from patients.

Patient characteristics

We used the VA Vital Status File to ascertain patients' age at cohort entry (categorized as <45 years then in 5-year increments up to 85 years), race (categorized as white, black and other), and sex. We used the VA Decision Support System Laboratory Results File to ascertain serum creatinine measures, and eGFR was estimated using the Modification of Diet in Renal Disease (MDRD) formula.[11] We used Medicare and VA administrative data to obtain information on outpatient nephrology clinic visits in the year before cohort entry and to identify the following comorbid conditions present at cohort entry based on International Classification of Disease Ninth Revision (ICD-9) diagnostic codes on at least two claims during the year before cohort entry: coronary artery disease

(ICD-9 410.0-414.9), congestive heart failure (ICD-9 398.91-404.93; 428.0-428.9), chronic obstructive pulmonary disease (ICD-9 491.0-493.22; 496.0; 518.1-518.2), cirrhosis (ICD-9 571.2-572.4), peripheral artery disease (ICD-9 443.9-445.02), hypertension (ICD-9 401.0-405.99; 997.91), diabetes mellitus (ICD-9 249.00-250.93), dementia (ICD-9 290.0-290.43; 291.2; 294.10-294.11; 331.0; 331.19; 331.82), cancer (ICD-9 140.0-234.9) and stroke (ICD-9 430.0-437.9). We also calculated a Gagne comorbidity score,[12] which combines the conditions included in the Charlson and Elixhauser comorbidity indices, to ascertain a comprehensive measure summarizing the overall burden of comorbidity for each patient at the time of cohort entry based on diagnostic codes in Medicare and VA administrative files during the preceding year. We then categorized patients as having a low (scores <4), moderate (scores 4-6) or high (scores >6) burden of comorbidity based on tertile of Gagne comorbidity score.

Outcome Measures

We used USRDS records and dialysis procedure code search of Medicare and VA administrative files to identify patients who were treated with RRT during follow-up. To understand the treatment status of cohort members who did not appear in USRDS and did not have a dialysis procedure code in administrative files during follow-up (n=9,403), we identified a random 25% sample (n=2,252) stratified by calendar year of cohort entry and VA service network for detailed medical record review (Figure 2).

Medical record review

The VA has a comprehensive national electronic medical record system that includes progress notes for all inpatient and outpatient encounters of patients receiving care at its facilities. All progress notes are available in Text Integration Utility (TIU) format through the VA Corporate Data Warehouse. Chart review was conducted using TIU notes in each patient's VA-wide electronic medical record from the time of cohort entry through death or October 1, 2011. To facilitate and enhance the completeness of chart review, we used Lucene text-searching software[13] to locate progress notes containing information about treatment decisions for advanced CKD. We used inclusive search queries that returned all discharge summaries, nephrology inpatient and outpatient progress notes, and all progress notes containing catch-all terms such as "dialysis," "end-stage renal disease" and "kidney disease." We further refined search queries to exclude invariant notes consisting of boilerplate questionnaires and assessment forms where search terms appeared.

We used a combined inductive and deductive approach to content analysis of the medical record.[14] Inductive content analysis is an unstructured approach to the reading of texts that facilitates identification of themes and patterns inherent to a phenomenon that have not been previously described. In deductive content analysis, reading of texts is aimed at determining whether they have attributes that are consistent with pre-defined themes and patterns. To accomplish this, two nephrologists (S.P.Y.W. and A.M.O.) reviewed the progress notes of 200 randomly selected patients in the sample to develop a coding schema to categorize patients into distinct groups reflecting their treatment status with respect to RRT at the time of most recent follow-up (i.e., received dialysis discussing and/or preparing for dialysis, decision against dialysis). The remaining 2,052

patients were selected for chart review to pre-specified treatment groups. Among those selected for chart review (n=2,252), we excluded from our analyses 207 with an eGFR at most recent follow-up in the medical record >15ml/min/1.73m^2 and 117 with insufficient documentation to characterize the clinical course of their CKD (Figure 1). To assess the validity of our coding framework, a senior nephrology fellow unconnected with the study independently reviewed the charts of 50 randomly selected patients included in the chart review. Agreement in assignment of patients to treatment groups between the initial and the independent reviewer was assessed using a weighted kappa statistic.

Analytical Approach

We combined patients with administrative record of having received RRT during follow-up based on USRDS enrollment or dialysis procedure code search of Medicare and VA files to serve as the referent category for in between-group comparisons. We used proportions, means and standard deviations, and chi-square and ANOVA tests where appropriate to compare the characteristics of patients in the referent category and those in the clinically distinct subgroups identified in the chart review sample. We assessed the characteristics associated with membership in each treatment group using a multinomial logistic regression model adjusted for age, race, sex, comorbidities, Gagne comorbidity burden score and calendar year at cohort entry, and number of nephrology outpatient visits in the year prior to cohort entry.

To further evaluate for temporal differences in treatment practices, we calculated the incidence and risk of enrollment in USRDS or having a dialysis procedure code during follow-up associated with late (2005-2009) vs. early (2000-2004) cohort entry for

each age group using a Cox proportional hazard model adjusted race, sex, comorbidities and Gagne comorbidity burden score at cohort entry and number of nephrology outpatient visits in the year prior to cohort entry.

The results of chart review were used to estimate the proportion and 95% confidence interval (CI) of the overall cohort expected to belong to each treatment group (i.e. received dialysis discussing and/or preparing for dialysis, decision against dialysis). We compared the estimated distribution of treatment groups within each age group using multinomial logistic regression adjusting for all baseline patient characteristics and calendar year of cohort entry. In sensitivity analyses, we repeated this process after stratification by tertile of comorbidity score to evaluate for differences in treatment practices based on burden of comorbidity.

Construction of the analytic dataset and statistical analyses were performed using SAS v. 9 (Cary, NC) and SPSS v.19 (Somers, NY).

Results

Outcomes

Of the 28,568 members of this cohort, 18,231 (63.8%) patients were registered in USRDS and an additional 934 patients (3.3%) had at least one dialysis treatment based on dialysis procedure code search of Medicare and VA administrative files during follow-up (Figure 1). Median time to date of USRDS enrollment or first dialysis procedure code in administrative files was 0.6 years (interquartile range [IQR] 0.2-1.2).

For the 1,928 patients included in the in-depth chart review, median follow-up was 0.4 years (IQR 0.1-1.3). These patients were grouped as follows (Figure 2): 1) *Received dialysis* (n=437; 22.7%): patients with documentation in progress notes that

they had received at least one dialysis treatment despite not being registered in USRDS or having a dialysis procedure code in administrative files; 2) *Discussing and/or preparing for dialysis* (n=640; 33.2%): patients who had not started dialysis by the end of follow-up but were preparing for dialysis or engaged in on-going discussions with providers about whether to undergo dialysis; and, 3) *Decision against dialysis* (n=851; 44.1%): patients for whom an explicit or implicit decision not to pursue dialysis had been made by either the patient themselves, family members and/or providers. Representative quotations from the medical record used to assign patients to each of these categories are presented in Table 1. Over 2,699 person-years follow-up (mean follow-up 1.4±1.8 years), 1,749 (90.7%) sampled patients, and assigned categories reflect their treatment status at the time of death. Inter-rater agreement in assignment of patients to treatment groups for a random sample of 50 patients was very good (weighted kappa = 0.83).

Figure 2. Cohort derivation

(Abbreviations: eGFR, estimated glomerular filtration rate; USRDS, United States Renal Data System; VA, Department of Veterans Affairs; RRT, renal replacement therapy)

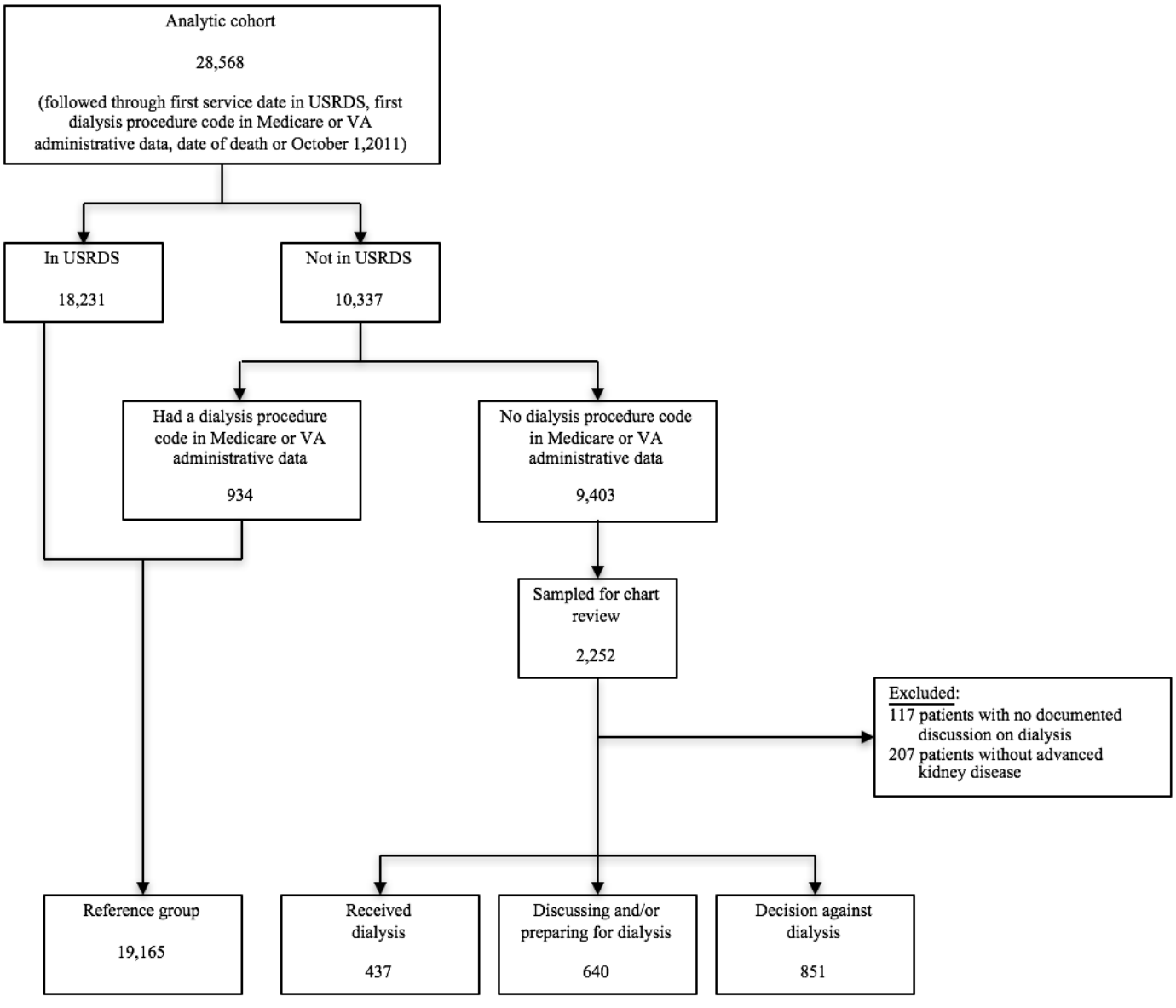


Table 1. Description of treatment subgroups within a sample of patients with advanced chronic kidney disease (N=1,928) identified through in-depth review of patients' medical record	
Clinical course	**Representative quotes abstracted from patients' medical record**
Received dialysis: Patients who were described in provider notes as having received at least one dialysis treatment but were not registered in the United States Renal Data System and did not have a dialysis procedure in Medicare or Veteran Affairs administrative data.	"patient had initiated on one course of hemodialysis...He then expressed his wishes that he did not want to utilize technology in the form of hemodialysis to maintain his life in its current status...he has chosen to pursue hospice"
	"Patient was dialyzed 3 times starting on September 10...Patient was found pulseless and apneic in the morning of September 13."
	"Patient did have [a] history of renal failure requiring hemodialysis twice several months ago at an outside hospital. Patient [is] unsure of [the] details."
***Discussing and/ or preparing for dialysis*:** Patients and/or their family members were discussing or preparing for the possibility of dialysis but had not yet started dialysis by the end of follow-up	"he verbalized moderate anxiety about making decision about dialysis. He does not know if he wants dialysis."
	"as the long-term plan, patient prefers peritoneal dialysis"
	"All three options (hemodialysis, peritoneal dialysis and renal transplant) were discussed with the patient in detail…Patient needs more time to think about it."
	"he has a fistula in left arm just in case he has to go on to dialysis"
***Decision against dialysis*:** Patients and/or their family members and providers made an explicit or implicit decision to not pursue dialysis	"Again discussed dialysis with patient's brother and power of attorney who declined dialysis"
	"has been seen by nephrology multiple times in the past and has repeatedly refused consideration for dialysis"
	"not a candidate for dialysis--demented, end stage acquired immune deficiency syndrome (AIDS), not on highly active antiretroviral therapy (HAART), dialysis wouldn't prolong life"
	"man with multiple medical problems including disseminated T cell lymphoma, congestive heart failure, renal failure…now receiving palliative care…not a dialysis candidate as patient [is] hospice"

Patient Characteristics

Compared with the referent group of patients who had received RRT based on enrollment in USRDS or dialysis procedure code in administrative files, patients who had in fact received some dialysis based on chart review, those who were preparing for or discussing dialysis and those in whom a decision against dialysis had been made were older, less often black, had a higher burden of comorbidity and had less nephrology care in the year prior to cohort entry (Table 2).

Table 2. Characteristics of patients in each treatment group for advanced chronic kidney disease

Characteristics at cohort entry	Enrolled in USRDS or had a dialysis procedure code[a] (n=19,165)	Chart review[b] (n=1,928)			p-value[c]
		Received dialysis (n=437)	Discussing and/or preparing for dialysis (n=640)	Decision against dialysis (n=851)	
Mean age, years (SD)	65.4 (11.1)	68.3 (10.5)	68.4 (10.8)	75.0 (10.3)	<0.001
Race					
White	11133 (58.1)	241 (55.1)	363 (56.7)	567 (66.6)	
Black	6307 (32.9)	108 (24.7)	140 (21.9)	165 (19.4)	<0.001
Other	1725 (9.0)	8 (20.1)	137 (21.4)	119 (14.0)	
Sex					
Female	302 (1.6)	4 (0.9)	8 (1.3)	9 (1.1)	0.40
Male	1863 (98.4)	433 (99.1)	632 (98.8)	842 (98.9)	
Mean Gagne comorbidity score (SD)	4.3 (2.4)	5.9 (2.7)	5.1 (2.8)	6.1 (3.0)	<0.001
Comorbidities					
Hypertension	5440 (28.4)	199 (45.5)	219 (34.2)	354 (41.6)	<0.001
Coronary artery disease	7062 (36.8)	211 (48.3)	280 (43.8)	386 (45.4)	<0.001
Congestive heart failure	5440 (28.4)	199 (45.5)	219 (34.2)	354 (41.6)	<0.001
Diabetes mellitus	11950 (62.4)	254 (58.1)	340 (53.1)	446 (52.4)	<0.001
Peripheral artery disease	2439 (12.7)	75 (17.2)	96 (15.0)	142 (16.7)	<0.001
Cancer	3114 (16.2)	109 (24.9)	169 (26.4)	273 (32.1)	<0.001
Chronic obstructive pulmonary disease	2749 (14.3)	126 (28.8)	151 (23.6)	241 (28.3)	<0.001
Dementia	239 (1.2)	17 (3.9)	19 (3.0)	75 (8.8)	<0.001
Stroke	1458 (7.6)	31 (7.1)	63 (9.8)	109 (12.8)	<0.001
Cirrhosis	202 (1.1)	19 (4.3)	16 (2.5)	17 (2.0)	<0.001
Mean nephrology clinic visits in year prior (SD)	4.4 (4.1)	3.8 (3.2)	3.8 (3.4)	3.5 (4.8)	<0.001

Abbreviations: USRDS, United States Renal Data System; SD, standard deviation
Values presented as n (%) except for where indicated
[a] in Medicare or Veteran Affairs administrative files; [b] of a random sample of patients who were not enrolled in USRDS during follow up nor had a dialysis procedure code during follow up; [c] corresponds to Chi-square or ANOVA tests where appropriate.

These differences persisted in adjusted analyses (Table 3). For instance, patients in whom there was a decision not to pursue dialysis were more often aged ≥75 years (61.3% vs. 24.6%, adjusted odds ratio [aOR] 5.83, 95% CI 4.74-7.17), were less often black (19.4% vs 32.9%, aOR 2.17, 95% CI 1.74-2.72), and had a high burden of comorbidity (42.1% vs. 18.9%, aOR 3.07, 95% CI 2.42-3.90) as compared with patients who received RRT,

even after adjusting for baseline patient characteristics. Certain comorbidities including cancer (32.1% vs. 16.2%, aOR 1.40, 95% CI 1.19-1.65), dementia (8.8% vs 1.2%, aOR 3.41, 95% CI 2.53-4.60), stroke (12.8% vs. 7.6%, aOR 1.40 (1.11-1.75), and cirrhosis (2.0% vs. 1.1%, aOR 1.91, 95%CI 1.11-3.29) were also more prevalent among patients in whom there was a decision against dialysis versus patients who had received RRT.

Table 3. Characteristics associated with each treatment group for advanced kidney disease[a]

Characteristics at cohort entry	Received dialysis by chart review aOR[b] (95% CI)	Discussing or preparing for dialysis aOR[b] (95% CI)	Decision against dialysis aOR[b] (95% CI)
Age			
<65 years	ref	ref	ref
65-74 years	1.65 (1.29-2.11)	1.32 (1.07-1.63)	2.08 (1.65-2.63)
≥75 years	1.44 (1.11-1.86)	1.46 (1.19-1.80)	5.83 (4.74-7.17)
Race			
White	ref	ref	ref
Black	0.98 (0.77-1.24)	0.81 (0.66-0.99)	0.70 (0.58-0.84)
Other	2.87 (2.20-3.76)	2.98 (2.40-3.70)	2.17 (1.74-2.72)
Male (vs. female) sex	1.47 (0.54-4.01)	1.14 (0.56-2.35)	1.00 (0.50-2.02)
Burden of comorbidity			
Low	ref	ref	ref
Moderate	1.99 (1.51-2.64)	1.35 (1.10-1.66)	1.54 (1.26-1.89)
High	3.38 (2.43-4.71)	1.64 (1.25-2.15)	3.07 (2.42-3.90)
Comorbidities			
Hypertension	0.84 (0.56-1.26)	0.75 (0.54-1.04)	0.54 (0.42-0.70)
Coronary artery disease	1.13 (0.90-1.40)	1.15 (0.96-1.38)	0.86 (0.73-1.01)
Congestive heart failure	1.19 (0.94-1.52)	0.98 (0.80-1.21)	1.03 (0.86-1.23)
Diabetes mellitus	0.68 (0.55-0.84)	0.64 (0.54-0.76)	0.78 (0.67-0.91)
Peripheral artery disease	1.01 (0.77-1.32)	1.01 (0.80-1.28)	0.94 (0.77-1.15)
Cancer	1.28 (1.01-1.630	1.50 (1.23-1.82)	1.40 (1.19-1.65)
Chronic obstructive pulmonary disease	1.47 (1.17-1.86)	1.42 (1.16-1.75)	1.33 (1.11-1.58)
Dementia	1.99 (1.18-3.36)	1.68 (1.03-2.76)	3.41 (2.53-4.60)
Stroke	0.71 (0.48-1.03)	1.16 (0.88-1.52)	1.40 (1.11-1.75)
Cirrhosis	2.98 (1.78-4.97)	1.84 (1.07-3.15)	1.91 (1.11-3.29)
≥4 (vs. <4) nephrology clinic visits in year prior	0.40 (0.32-0.50)	0.54 (0.45-0.65)	0.32 (0.26-1.09)

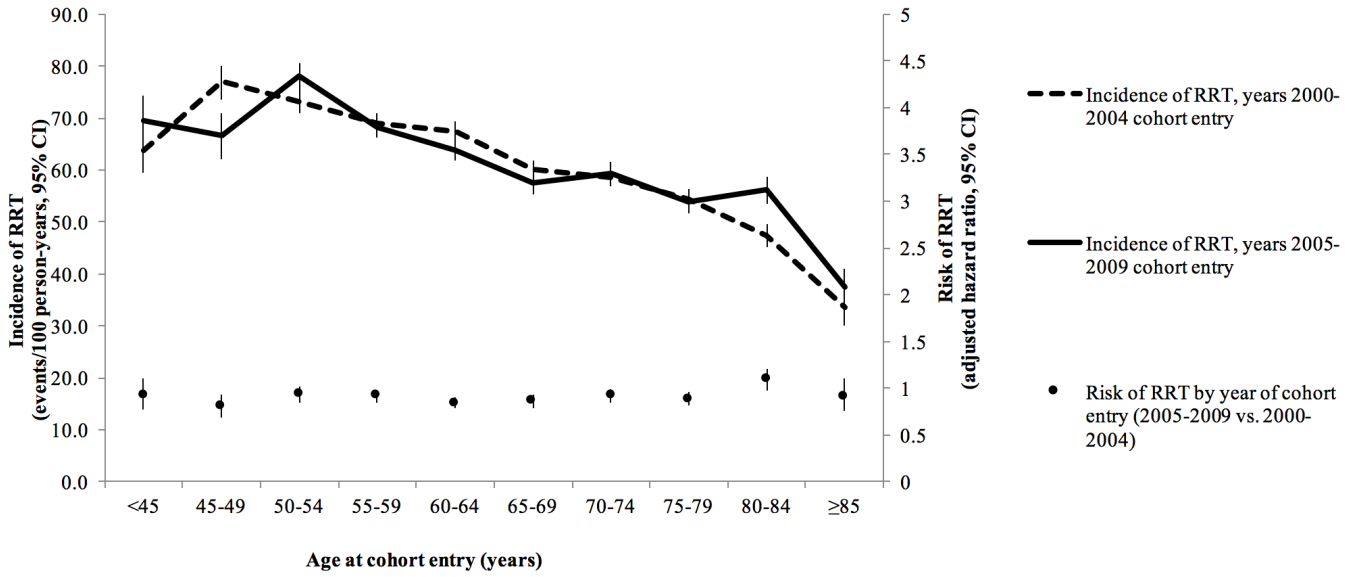
Abbreviations: aOR, adjusted odds ratios; CI, confidence interval

[a] multinomial logistic regression model adjusted for age, race, sex, comorbidity burden, comorbidities, prior nephrology care, and year of cohort entry

[b] reference group are patients who were enrolled in the United States Renal Data System or had a dialysis procedure code in Medicare or Veteran Affairs administrative files

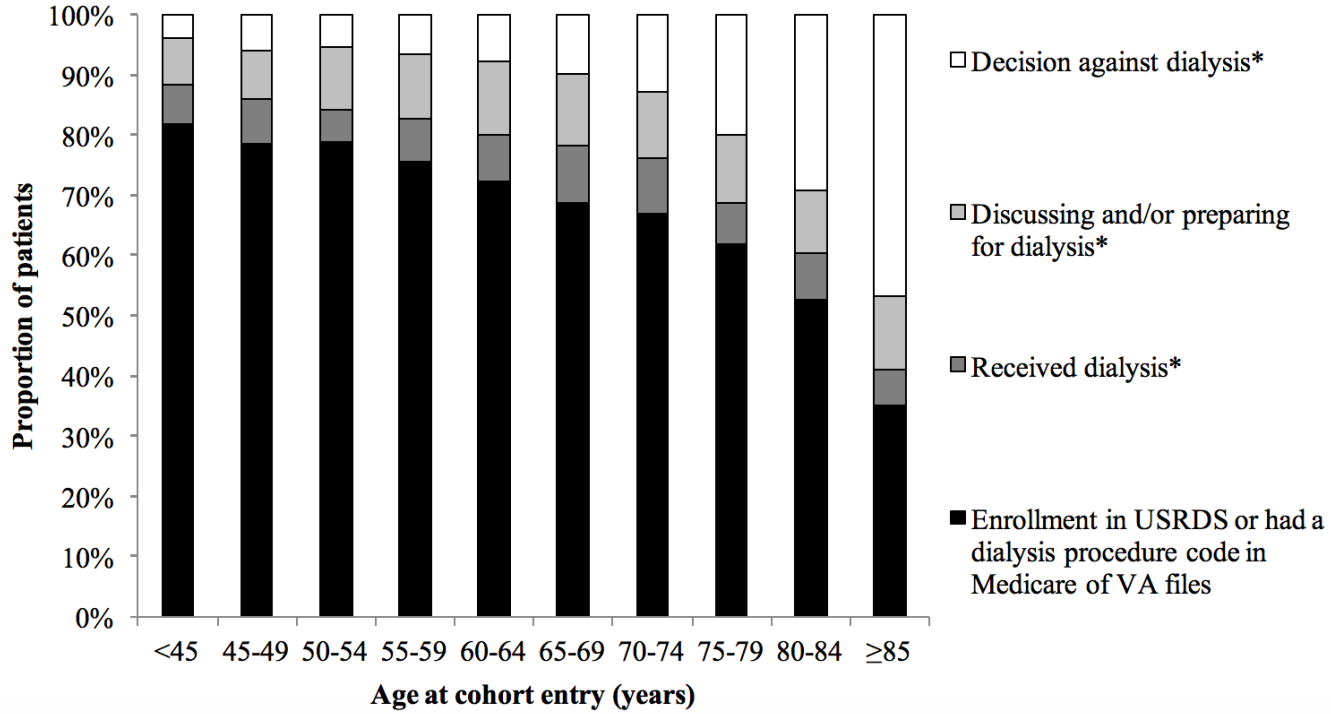
The incidence of RRT based on enrollment in USRDS or dialysis procedure code in administrative files for cohort members in each age group was similar for those who entered the cohort earlier (2000-2004) versus later (2005-2009) in time (Figure 3).

Figure 3. Temporal differences in incidence and risk[a] of treatment with renal replacement therapy (RRT)[b] between 2000-2004 and 2005-2009.
([a] cox proportional hazard model adjusted for sex, race, comorbidities, comorbidity burden and prior nephrology care, [b] based on enrollment in the United States Renal Data System or having a dialysis procedure code in Medicare or Veterans Affairs administrative files)



Based on chart review for this random sample of patients, we estimate that the proportion of all cohort members who received RRT or were preparing for or discussing dialysis decreased linearly with age from 96.2% (95% CI 94.4-97.4) among patients aged <45 years to 53.3% (95% CI 50.7-55.9) among patients aged ≥85 years (adjusted trend, p-value <0.001) (Figure 4). Conversely, the decision not to pursue dialysis was more common at older ages, increasing from an estimated 3.8% (95% CI 2.6-5.6) among patients aged <45 years to 46.7% (95% CI 44.1-49.3) among patients aged ≥85 years (adjusted trend, p-value <0.001).

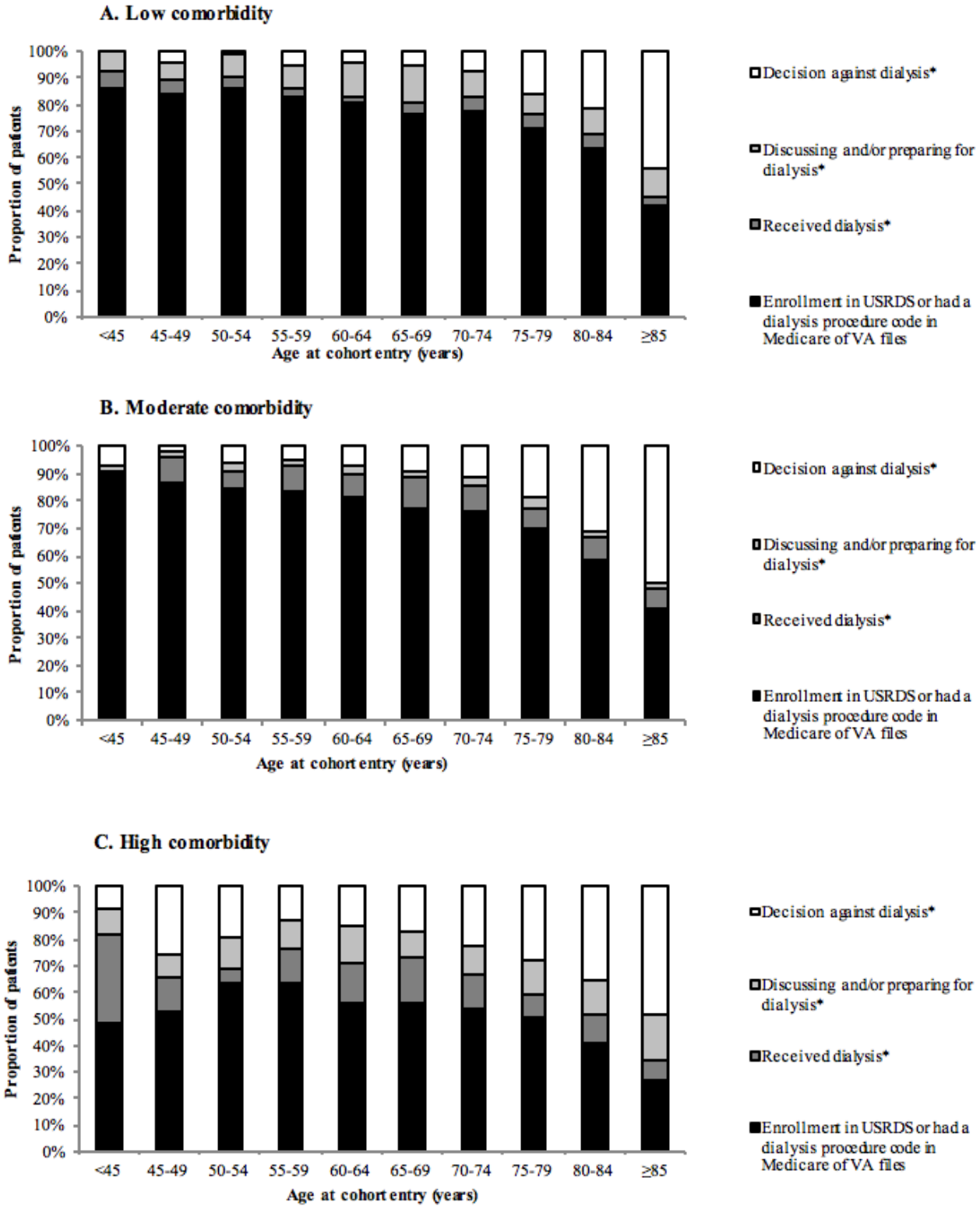
Figure 4. Age differences in treatment decisions and practices for advanced kidney disease
(Abbreviations: USRDS, United States Renal Data System; VA, Department of Veteran Affairs; * based on chart review of a random sample of patients who were not enrolled in USRDS and did not have a dialysis procedure code in Medicare or VA administrative files during follow-up)



Analyses of the age distribution of RRT decisions stratified by tertile of comorbidity score were broadly consistent with the non-stratified analyses (Figure 5). For example, for patients aged ≥85 years, the estimated proportion of patients in whom a decision against dialysis had been made was similar for those in the lowest (44.5%, 95% CI 39.5-49.6) vs. highest (48.8%, 95% CI 44.4-53.3) tertile of comorbidity (unadjusted p=0.60).

Figure 5. Age differences in treatment decisions and practices for advanced kidney disease, stratified by comorbidity score[a]

(Abbreviations: USRDS, United States Renal Data System; VA, Department of Veteran Affairs; [a] based on tertile of Gagne comorbidity score; * based on chart review of a random sample of patients who were not enrolled in USRDS and did not have a dialysis procedure code in Medicare or VA administrative files during follow-up)

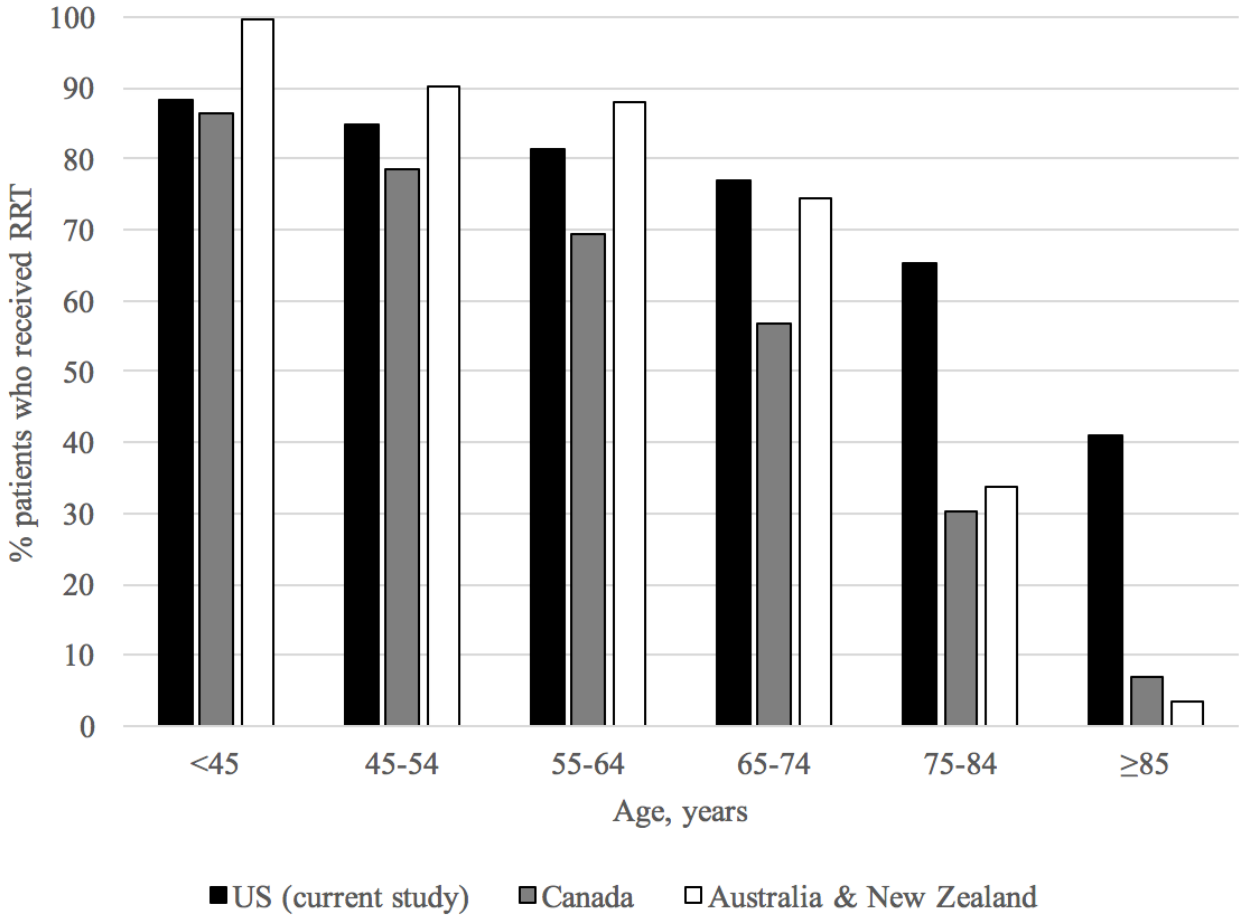


Discussion

Among a national cohort with advanced CKD receiving care in the VA, most patients were enrolled in USRDS (63.8%) or had a dialysis procedure code in VA or Medicare administrative files (3.3%) during follow-up. Based on in-depth chart review of a random sample of the patients who were did not have administrative record of having received RRT, we estimate that an additional 7.5% of cohort members had in fact received at least one dialysis treatment not captured in administrative data. An additional 10.9% were discussing and/or preparing for dialysis but had not yet started dialysis at end of follow-up. Thus, at most recent follow-up, the overwhelming majority (85.5%) of patients had either received--or were preparing to receive--RRT. In only 14.5% of cohort members was there an implicit or explicit decision not to pursue dialysis.

The proportion of patients in this cohort who were treated with RRT is higher than previously reported for other developed nations.[8,9] In a large retrospective study conducted in Canada using registry and administrative records from 2002-2008,[8] Hemmelgarn et al. found that 51.4% of patients who developed kidney failure (defined as a sustained eGFR <15 ml/min/1.73m^2 or receipt of dialysis or kidney transplant) were treated with RRT. In a retrospective study using registry and death certificate data from New Zealand and Australia between 2003-2007,[9] Sparke et al. reported that 51.2% of patients with kidney failure (defined as either enrollment in the RRT registry or death from kidney disease without receipt of dialysis or kidney transplant) received RRT.

Figure 6. International differences in utilization of renal replacement therapy (RRT) among patients with advanced chronic kidney disease. (see citations 7 and 8 for original data for Canada and Australia and New Zealand, respectively)



Differences in the use of RRT between our study compared with these earlier studies are much more striking for older than for younger age groups (Figure 6). The percentage of patients aged <45 years treated with RRT in our cohort (88.4%) was similar to that reported by Hemmelgarn et al. (86.3%)[8] and Sparke et al. (>95.0%).[9] However, at older ages, the proportion treated with RRT was far higher for members of our cohort. Despite the fact that life expectancy is severely limited in older patients who initiate chronic dialysis,[5] 41.1% of patients aged ≥85 years in our cohort were treated with RRT. In comparison, only 6.8% and <5.0% of similarly aged patients had received

RRT in cohorts described by Hemmelgarn et al.[8] and Sparke et al.,[9] respectively. Burden of comorbidity is also a key determinant of prognosis in patients who initiate dialysis. Observational studies conducted outside the US suggest that dialysis may not meaningfully extend life in older patients with significant comorbidity.[15-19] It is also associated with poorer quality of life as compared with more conservative measures, such as hospice and palliative care.[20] Although decisions against dialysis were generally more common among patients with higher burden of comorbidity, burden of comorbidity did not seem to play an important role in mediating decisions about RRT among older patients. Even among members of the oldest age group with the highest burden of comorbidity, most received or were preparing to receive RRT at last follow-up. Patients with a higher vs. lower burden of comorbidity were also more likely to still be preparing for RRT at most recent follow-up, which might suggest that dialysis had been recommended in these patients for whom the competing risk of death may have exceeded their risk of developing a need to initiate RRT. These findings are consistent with the observation that the incidence rate of RRT in the US greatly surpasses that reported for European populations with a similar prevalence of advanced CKD and other significant chronic illness.[4] In a survey study of US nephrologists, a minority reported that they would offer conservative therapy and palliative care as an alternative to RRT to older patients with multimorbidity.[21]

Taken in this context, our findings reiterate concerns that, in the US, decisions about RRT may not be strongly guided by the individual considerations and preferences of patients. Prior qualitative studies indicate that dialysis tends to be framed to patients as "inevitable" rather than as a true treatment "choice."[22-24] Clinical practice guidelines

recommend that decisions about dialysis integrate patients' values, goals and preferences and physicians' expertise on prognosis and the distinct risks and benefits of dialysis for individual patients.[10,25] However, recent studies indicate that trends in dialysis practices seem driven more by health system and physician factors, such as regional patterns of healthcare expenditure or practice styles favoring use of interventions intended to lengthen life.[22,26,27]

There were other notable differences in RRT practices across patient subgroups. Use of RRT was more common and decisions against dialysis less common among black as compared with white patients. This finding is in agreement with prior studies reporting greater use of other potentially life-sustaining treatments, such as cardiopulmonary resuscitation and mechanical ventilation, and less frequent use of hospice among black as compared with white patients with and without advanced CKD.[26,28,29] Greater use of RRT among black versus white patients has been variously attributed to racial differences in burden of CKD,[30] access to kidney transplant and competing risk of death during the advanced stages of kidney disease,[31] and attitudes toward artificial life-prolongation.[32] Use of RRT was also less common and decisions against dialysis more common among patients with histories of dementia, stroke, cancer and cirrhosis. This finding seems consistent with other studies in which nephrologists reported viewing dialysis as undesirable in circumstances of severe cognitive and/or functional impairment or terminal illness from another condition.[33-36]

To the best of our knowledge, this is the first study to measure the proportion of patients with advanced CKD who received and did not receive RRT, and the disparities in use of RRT between patient subgroups and across different countries. An additional

strength of our study is that we leveraged the VA-wide electronic medical record to clarify the treatment status of patients who did not receive RRT during follow-up and whether patients had desired but did not receive dialysis or if there was a decision not to pursue dialysis. We also adopted a rigorous approach to capturing episodes of dialysis occurring within the VA, at non-VA facilities but paid for by the VA, and under fee-for-service Medicare.

However, this study also has several limitations. First, the study population only included US military veterans, who are predominantly white, male patients, and to veterans who underwent serum creatinine measurement at a VA facility. Thus, our study may not be generalizable to those receiving care in other health systems or to other US populations with advanced CKD. Prior work suggest dialysis initiation practices are more conservative within versus outside the VA. For instance, one study reported that the mean eGFR (or level of kidney function) of patients at which chronic dialysis is initiated at a VA facility is lower than that found among patients who initiate therapy at a non-VA facility.[37] Therefore, we suspect that the proportion of patients treated with RRT in this study is probably lower than would be expected for members of the general US population with advanced CKD. Second, differences in study design argue for caution in comparing rates of RRT in our study with those reported in prior studies conducted outside the US.[8,9] Our definition of advanced CKD and method for identifying RRT were similar to those used by Hemmelgarn et al,[8] however Sparke et al[9] restricted their definition of patients who did not receive RRT as those who died and did not receive RRT whereas we included in our analyses patients were living and had not received RRT at end of follow-up. If patients who were living at end of follow-up would have

ultimately received RRT, the rate of RRT for our study cohort would be even higher. The proportion of patients treated with RRT is also likely sensitive to exclusion and inclusion criteria such as the threshold level of eGFR and requirement for chronicity. We chose to focus our study on patients with severe CKD (i.e, a sustained eGFR <15 ml/min/1.73 m^2) in order to examine treatment decisions and practices among those patients most likely to receive RRT. Treatment rates would almost certainly have been lower if we had selected a higher eGFR threshold and included patients with transient loss of eGFR. Third, we were not able to capture dialysis treatments paid for by Medicare Advantage or private insurance. Thus, our results likely underestimate the proportion of cohort members who received dialysis. Fourth, categorization of patients into treatment groups was based on documentation in the VA electronic medical record which might not fully or precisely capture the clinical context or attitudes towards dialysis held by individual patients. Categorization was also based on decisions documented at most recent follow-up and does not capture prior or changes in patients' preferences for dialysis during the course of their illness. Our study findings also cannot address the adequacy of patients' understanding of their treatment options and engagement in decision-making about RRT.

In this large national cohort of VA patients with advanced CKD, dialysis initiation practices among older patients were far more common than reported for other developed countries.[8,9] Our findings underscore the relevance of shared decision-making for dialysis to ensure that treatment decisions uphold the priorities and preferences of individual patients and their families, as well as being grounded in realistic expectations about prognosis and the expected benefits and harms of this treatment.

Acknowledgements

We thank Pamela Green, Margaret Yu and Christine Sulc for their assistance with data programming, chart review, and study coordination, respectively, for this study. This work was supported by VA Health Services Research and Development grants (IIR 09-094, PI Hebert; and IIR 12-126, PI O'Hare) and an Interagency Agreement between the VA Puget Sound and the Centers for Disease Control and Prevention (IAA 15FED1505101-0001; PI O'Hare). During the completion of this work, I was supported by the Clinical Scientist in Nephrology Fellowship from the American Kidney Fund. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position or policy of the Centers for Disease Control and Prevention or the VA. Portions of this work were published in the Clinical Journal of the American Society of Nephrology,[38] who granted permission to use the material for this thesis.

References

1. United States Renal Data System. 2015 USRDS annual data report: epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2015.
2. ERA-EDTA Registry Annual Report 2013. Academic Medical Center, Department of Medical Informatics, Amsterdam, The Netherlands, 2015.
3. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. JAMA 2007; 298: 2038-47.
4. Hallan SI, Coresh J, Astor BC, et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. J Am Soc Nephrol 2006; 17:2275-84.
5. Kurella M, Covinsky KE, Collins AJ, Chertow GM. Octogenarians and nonagenarians starting dialysis in the United States. Ann Intern Med. 2007; 146:177-183.
6. Treit K, Lam D, O'Hare AM. Timing of dialysis initiation in the geriatric population: toward a patient-centered approach. Semin Dial 2013; 26: 682-9.
7. Bowling CB & Mutner P. Epidemiology of chronic kidney disease among older adults: a focus on the oldest old. J Gerontol A Biol Sci Med Sci 2012; 67: 1379-86.
8. Hemmelgarn BR, James MT, Manns BJ, et al. Rates of treated and untreated kidney failure in older vs. younger adults. JAMA 2012; 307:2507-15.
9. Sparke C, Moon L, Green F, et al. Estimating the total incidence of kidney failure In Australia including individuals who are not treated by dialysis or transplantation. Am J Kidney Dis 2013; 61:413-9.

10. National Kidney Foundation. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Am J Kidney Dis 2002; 39: S1-266.
11. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999; 130: 461-70.
12. Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol 2011; 64: 749-59.
13. Hammond KW, Laundry R, O'Leary TM, Jones WP. Use of text search to effectively identify lifetime prevalence of suicide attempts among veterans. System Sciences (HICSS), 2013 46th Hawaii International Conference on System Sciences: pg 2672-2683.
14. Krippendorff K. Content analysis: an introduction to its methodology. 3rd Ed. Thousand Oaks (CA): Sage Publications; 2013.
15. Murtagh FE, Marsh JE, Donohoe P, Ekbal NJ, Sheerin NS, Harris FE. Dialysis or not? A comparative survival study of patients over 75 years with chronic kidney disease stage 5. Nephrol Dial Transplant 2007; 22:1955-62.
16. Chandna SM, Shulz J, Lawrence C, Greenwood RN, Farrington K. Is there a rationale for rationing chronic dialysis? A hospital based cohort study of factors affecting survival and morbidity. BMJ 1999, 318:217-23.

17. Smith C, Da Silva-Gane M, Chandna S, Warwicker P, Greenwood R, Farrington K. Choosing not to dialyse: evaluation of planned non-dialytic management in a cohort of patients with end-stage renal failure. Nephron Clin Pract 2003; 95:c40-6.
18. Hussain JA, Mooney A, Russon L. Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. Palliat Med 2013; 27:829-939.
19. Carson RC, Juszczak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? Clin J Am Soc Nephrol 2009; 4:1611-9.
20. Da Silva-Gane M, Wellsted D, Greenshields H, Norton S, Chandna SM, Farrington K. Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. Clin J Am Soc Nephrol 2012; 7: 2002-9.
21. Parvez S, Abdel-Kader K, Pankratz S, Unruh M. Provider knowledge, attitudes and practices surrounding conservative management for patients with advanced CKD. Clin J Am Soc Nephrol 2016; 11:812-20.
22. Wong SP, Vig EK, Taylor JS, Burrows NR, Liu CF, Williams DE, Hebert PL, O'Hare AM. Timing of initiation of maintenance dialysis: a qualitative analysis of the electronic medical records of a national cohort of patients form the Department of Veteran Affairs. JAMA Intern Med 2016; 176: 228-35.
23. Kaufman SR. Ordinary medicine: extraordinary treatments, longer lives and where to draw the line. London: Duke University Press, 2015.

24. Schell JO, Patel UD, Steinhauser KE, Ammarell N, Tulsky JA. Discussions of the kidney disease trajectory by elderly patients and nephrologists: a qualitative study. Am J Kidney Dis. 2012;59: 495-503.
25. Renal Physicians Association. Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis, 2nd ed., Rockville, MD: Renal Physicians Association, 2010.
26. Wong SP, Kreuter W, O'Hare AM. Treatment intensity at the end of life in older adults receiving long-term dialysis. Arch Intern med 2012; 172:661-3.
27. O'Hare AM, Rodriguez RA, Hailpern SM, Larson EB, Tamura MK. Regional variation in health care intensity and treatment practices for end-stage renal disease in older adults. JAMA 2010; 304:180-6.
28. Wong SP, Kreuter W, Curtis JR, Hall YN, O'Hare AM. Trends in in-hospital cardiopulmonary resuscitation and survival in adults receiving maintenance dialysis. JAMA Intern Med 2015; 175: 1028-35.
29. Thomas BA, Rodriguez RA, Boyko EJ, Robinson-Cohen C, Fitzpatrick AL, O'Hare AM. Geographic variation in black-white differences in end-of-life care for patients with ESRD. Clin J Am Soc Nephrol 2013; 8: 1171-8.
30. Robinson BM, Joffe MM, Pisoni RL, Port FK, Feldman HI. Revisiting survival differences by race and ethnicity among hemodialysis patients: the Dialysis Outcomes and Practice Patterns Study. J Am Soc Nephrol. 2006;17:2910-2918.
31. Kucirka LM, Grams ME, Lessler J, et al. Association of race and age with survival among patients undergoing dialysis. JAMA. 2011;306: 620-626.

32. Searight HR & Gafford J. Cultural diversity at the end of life: issues and guidelines for family physicians. Am Fam Physician 2005; 71:515-22.
33. Sekkarie M, Cosma M, Mendelssohn D. Nonreferral and nonacceptance to dialysis by primary care physicians and nephrologists in Canada and the United States. Am J Kidney Dis 2001; 38: 36-41.
34. McKenzie JK, Moss AH, Stocking CB, Siegler M. Dialysis decision making in Canada, the United Kingdom and the United States. Am J Kidney Dis 1998; 31: 12-8.
35. Sekkarie MA, Moss AH. Withholding and withdrawing dialysis: the role of physician specialty and education and patient functional status. Am J Kidney Dis 1998; 31:464-72.
36. Halvorsen K, Stettebo A, Nortvedt P, et al. Priority dilemmas in dialysis: the impact of old age. J Med Ethics 2008; 34: 585-9.
37. Yu MK, O'Hare AM, Batten A, et al. Trends in timing of dialysis initiation within versus outside the Department of Veteran Affairs. Clin J Am Soc Nephrol 2015; 10:1418-27.
38. Wong SP, Hebert PL, Laundry RJ, et al. Decisions about renal replacement therapy in patients with advanced kidney disease in the US Department of Veterans Affairs, 2000-2011. Clin Am J Son Nephrol 2016; pii.CJN.03760416