

# Trends in the Timing and Clinical Context of Maintenance Dialysis Initiation

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## ABSTRACT

Whether secular trends in eGFR at dialysis initiation reflect changes in clinical presentation over time is unknown. We reviewed the medical records of a random sample of patients who initiated maintenance dialysis in the Department of Veterans Affairs (VA) in fiscal years 2000–2009 ( $n=1691$ ) to characterize trends in clinical presentation in relation to eGFR at initiation. Between fiscal years 2000–2004 and 2005–2009, mean eGFR at initiation increased from  $9.8 \pm 5.8$  to  $11.0 \pm 5.5$  ml/min per  $1.73 \text{ m}^2$  ( $P < 0.001$ ), the percentage of patients with an eGFR of 10–15 ml/min per  $1.73 \text{ m}^2$  increased from 23.4% to 29.9% ( $P = 0.002$ ), and the percentage of patients with an eGFR  $> 15$  ml/min per  $1.73 \text{ m}^2$  increased from 12.1% to 16.3% ( $P = 0.01$ ). The proportion of patients who were acutely ill at the time of initiation and the proportion of patients for whom the decision to initiate dialysis was based only on level of kidney function did not change over time. Frequencies of documented clinical signs and/or symptoms were similar during both time periods. The adjusted odds of initiating dialysis at an eGFR of 10–15 or  $> 15$  ml/min per  $1.73 \text{ m}^2$  (versus  $< 10$  ml/min per  $1.73 \text{ m}^2$ ) during the later versus earlier time period were 1.43 (95% confidence interval [95% CI], 1.13 to 1.81) and 1.46 (95% CI, 1.09 to 1.97), respectively. In conclusion, trends in eGFR at dialysis initiation at VA medical centers do not seem to reflect changes in the clinical context in which dialysis is initiated.

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For more than a decade, there has been a pervasive upward trend in the level of eGFR at initiation of maintenance dialysis both within and outside the United States.<sup>1–5</sup> The driving forces behind this trend are not well understood. One hypothesis is that trends in eGFR at initiation may signal greater reliance on eGFR versus clinical signs and/or symptoms in deciding when to initiate dialysis.<sup>1</sup> Some studies have suggested that changes in the guideline-recommended approach to CKD in the early 2000s—including methods for assessing the severity of CKD and automated reporting of eGFR—may have inadvertently encouraged earlier dialysis initiation in asymptomatic patients based only on their level of eGFR.<sup>1,3,6,7</sup> Arguing against this possibility, a recent Canadian study found no evidence that widespread eGFR reporting has led to earlier dialysis initiation.<sup>7</sup> A second hypothesis is that there may have been

changes over time in indications for dialysis not captured in available data sources,<sup>8–10</sup> although stable levels of health care intensity around the time of dialysis initiation among Medicare beneficiaries do not seem to support this possibility.<sup>11</sup> A third hypothesis is that trends in eGFR at initiation may reflect a progressive liberalization of guideline criteria for dialysis initiation from the late 1990s onward to promote initiation at higher levels of eGFR, especially among patients with relatively soft uremic signs and

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symptoms.<sup>1,12</sup> Because prior studies have relied on data sources that did not include detailed information on clinical presentation at the time of initiation, little evidence is available to either support or refute the role of changing clinical indications for dialysis over time.<sup>1–5,13</sup> To address this knowledge gap, we designed a study using detailed information from the system-wide electronic medical record of the Department of Veterans Affairs (VA) to examine temporal trends in eGFR in relation to the clinical context of dialysis initiation.

## RESULTS

Cohort members who initiated dialysis in fiscal years (FYs) 2005–2009 were, on average, older and more likely to be white compared with those who initiated dialysis in FYs 2000–2004 (Table 1). Patients who initiated dialysis during the more recent time period had a higher prevalence of diabetes, a higher median risk score, and a similar prevalence of other comorbid conditions compared with those who initiated dialysis in the earlier time period. Median eGFR slope and number of visits to a VA nephrologist during the year before initiation were also similar across time periods. Patients initiating hemodialysis during the more recent time period were more likely to do so with an arteriovenous fistula.

There were no significant changes over time in the percentage of patients who were acutely ill—that is, hospitalized for sudden

decline in clinical status—at the time of dialysis initiation (49.8% versus 49.7%;  $P=0.99$ ) or the percentage for whom the decision to appear to be based only on their level of estimated kidney function (4.5% versus 5.8%;  $P=0.23$ ). Most patients who were not acutely ill at the time of initiation had one or more signs and/or symptoms consistent with advanced kidney disease that were either stable or gradually worsening. There were no statistically significant differences over time in the types of clinical signs and/or symptoms documented around the time of initiation, with gastrointestinal and cardiopulmonary signs and/or symptoms being the most frequently documented during both time periods (Figure 1). Most patients had documented signs and/or symptoms in at least two different categories (median=2; interquartile range=1–3 in both time periods).

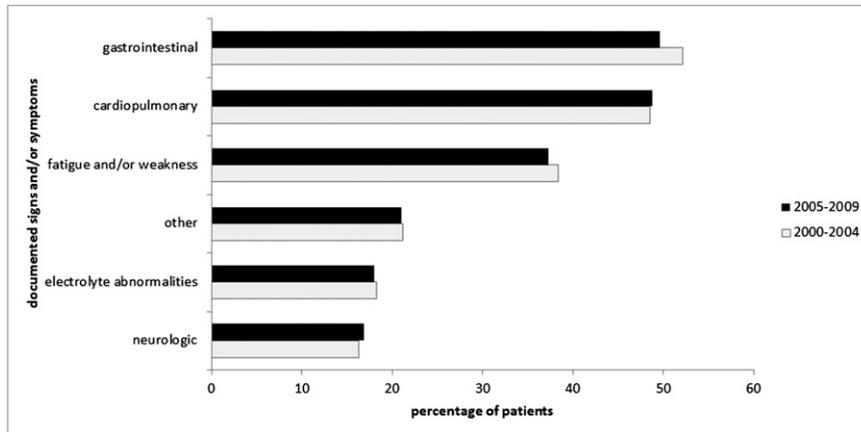
From 2000–2004 to 2005–2009, mean eGFR at dialysis initiation increased from  $9.8 \pm 5.8$  to  $11.0 \pm 5.5$  ml/min per  $1.73 \text{ m}^2$  ( $P<0.001$ ), the percentage of patients with an eGFR=10–15 ml/min per  $1.73 \text{ m}^2$  increased from 23.4% to 29.9% ( $P=0.002$ ), and the percentage with an eGFR>15 ml/min per  $1.73 \text{ m}^2$  increased from 12.1% to 16.3% ( $P=0.01$ ). After stratification by illness acuity and types of signs and/or symptoms, there was a statistically significant increase in mean eGFR at initiation over time for all subgroups.

After adjustment for illness acuity, documented clinical signs and/or symptoms, and patient characteristics at the time of initiation, the odds of initiating dialysis at an eGFR=10–15

**Table 1.** Patient characteristics by time period of initiation

	Year of Initiation		P Value
	2000–2004 (n=826)	2005–2009 (n=865)	
Age (SD), yr	62.0 (11.4)	63.5 (11.1)	0.003
Nonwhite race, %	47.3	40.4	0.004
Women, %	1.3	2.0	0.31
Diabetes, %	56.5	66.5	<0.001
Ischemic heart disease, %	29.9	31.6	0.46
Congestive heart failure, %	29.5	32.8	0.14
Peripheral arterial disease, %	6.4	5.8	0.59
Stroke, %	4.5	5.3	0.43
Chronic obstructive pulmonary disease, %	15.0	16.3	0.47
Median risk score (25th, 75th percentiles)	2.0 (1.3, 2.9)	2.3 (1.5, 3.2)	<0.001
Died within 1 yr of initiation, %	17.1	15.4	0.35
Mean eGFR at initiation (SD), ml/min per $1.73 \text{ m}^2$	9.8 (5.8)	11.0 (5.5)	<0.001
Median interval between most recent eGFR and initiation (25th, 75th percentiles), d	2 (1, 6)	1 (1, 7)	0.71
Median eGFR slope (25th, 75th percentiles), <sup>a</sup> ml/min per $1.73 \text{ m}^2$ per yr	–13.7 (–7.4, –21.6)	–14.1 (–7.8, 24.2)	0.07
Inpatient initiation, %	74.9	74.6	0.86
Access used at initiation			
Peritoneal dialysis catheter, %	5.3	4.3	0.002
Hemodialysis fistula, %	16.3	21.9	
Hemodialysis graft, %	4.6	2.3	
Hemodialysis catheter, %	73.7	71.6	
Median outpatient VA nephrology visits <sup>a</sup> (interquartile range)	3 (0–6)	3 (1–6)	0.11

<sup>a</sup>During the year before initiation.



**Figure 1.** Distribution of documented clinical signs and/or symptoms at the time of initiation in 2000–2004 versus 2005–2009. There were no statistically significant differences between 2000–2004 and 2005–2009 in the prevalence of any of the groupings of clinical signs and/or symptoms.

and  $>15$  ml/min per  $1.73$  m<sup>2</sup> (versus  $<10$  ml/min per  $1.73$  m<sup>2</sup>) in 2005–2009 versus 2000–2004 were 1.43 (95% confidence interval, 1.13 to 1.81) and 1.46 (95% confidence interval, 1.09 to 1.97), respectively (Table 2). After stratification by illness acuity, there was an increased adjusted odds of initiating dialysis at an eGFR=10–15 ml/min per  $1.73$  m<sup>2</sup> (versus  $<10$  ml/min per  $1.73$  m<sup>2</sup>) in the more recent versus earlier time period for those who were acutely ill at the time of initiation but not for those who were not acutely ill. Conversely, there was an increased adjusted odds of initiating dialysis at an eGFR $>15$  ml/min per  $1.73$  m<sup>2</sup> (versus  $<10$  ml/min per  $1.73$  m<sup>2</sup>) in the more recent versus earlier time period for patients who were not acutely ill at the time of initiation but not for those who were acutely ill. After stratification by types of clinical signs and/or symptoms, there was a higher adjusted odds of initiating dialysis at an eGFR=10–15 ml/min per  $1.73$  m<sup>2</sup> in the more recent time period for those with cardiopulmonary and other signs and/or symptoms and a higher adjusted odds of initiating dialysis at an eGFR $>15$  ml/min per  $1.73$  m<sup>2</sup> among those with documented fatigue and/or weakness and gastrointestinal signs and/or symptoms.

## DISCUSSION

Between FYs 2000 and 2009, there was an upward trend in eGFR at initiation among a national cohort of patients for whom the decision to initiate dialysis was made within the VA system. This trend was not explained by changes in clinical presentation over time: neither the percentage of patients presenting with an acute illness nor the distribution of different types of clinical signs and/or symptoms at the time of dialysis initiation changed appreciably during this time period.

Our findings seem to indicate that dialysis initiation practices have changed over time to embrace higher threshold

levels of eGFR as being appropriate for dialysis initiation across a wide range of different clinical contexts. As for other populations, temporal trends in eGFR at initiation among members of this cohort did not seem to be driven by changes in case mix at the time of initiation.<sup>3</sup> Although patients who initiated dialysis during the later time period were older and had a higher burden of comorbidities than those who initiated dialysis during the earlier time period, the association of time period with level of eGFR at initiation persisted after adjustment for differences in patient characteristics. Detailed medical record review also provided no support for the hypothesis that an upward trend in eGFR at initiation reflected changes in clinical presentation at the time of dialysis initiation. Neither acuity level nor the types of clinical signs and/or

symptoms documented around the time of initiation changed appreciably over time, and the association between time period and eGFR at initiation was still present after adjustment for these aspects of the clinical presentation. Trends in eGFR at initiation also did not reflect a greater tendency to initiate dialysis in asymptomatic patients based only on their estimated level of kidney function. Although treatment decisions were occasionally driven by level of kidney function in the absence of other clinical signs and/or symptoms, this practice was no more common in recent compared with earlier years.

Although an upward trend in eGFR over time was present, regardless of illness acuity or types of documented signs and/or symptoms, there were notable differences in the magnitude of change in eGFR over time depending on clinical context. An increase in the percentage of patients initiating dialysis at very high levels of eGFR ( $>15$  ml/min per  $1.73$  m<sup>2</sup>) was present only among those who were not acutely ill at the time of initiation or had documented fatigue and/or weakness and gastrointestinal signs and/or symptoms. Among patients who were acutely ill or had cardiopulmonary signs and/or symptoms, there was an increase in the percentage with an eGFR=10–15 ml/min per  $1.73$  m<sup>2</sup> but not in the percentage with higher levels of eGFR. We suspect that a selective increase in the frequency of dialysis initiation at very high levels of eGFR among patients with softer indications for dialysis probably reflects the effect of changes in opinion-based clinical practice guidelines for dialysis initiation from the late 1990s onward. In 1997, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) guideline for peritoneal dialysis adequacy recommended that dialysis be initiated at a GFR of approximately 10.5 ml/min per  $1.73$  m<sup>2</sup>, except in the "complete absence of clinical signs and symptoms attributable to uremia."<sup>14</sup> The 2001 update of this guideline recommended dialysis initiation at GFR levels as high as 20 ml/min per  $1.73$  m<sup>2</sup>

**Table 2.** Relationship between time period of initiation, clinical presentation, and eGFR at initiation

Population	eGFR=10–15 ml/min per 1.73 m <sup>2</sup> , %	eGFR>15 ml/min per 1.73 m <sup>2</sup> , %	Adjusted Odds Ratio for 2005–2009 Versus 2000–2004 (95% Confidence Interval) <sup>a</sup>	
			eGFR=10–15 ml/min per 1.73 m <sup>2</sup>	eGFR>15 ml/min per 1.73 m <sup>2</sup> per yr
All patients (n=1691) <sup>b</sup>				
2000–2004	23.4	12.1	—	—
2005–2009	29.9	16.3	1.43 (1.13 to 1.81)	1.46 (1.09 to 1.97)
Acutely ill (n=841)				
2000–2004	19.7	14.8	—	—
2005–2009	29.3	15.6	1.65 (1.16 to 2.34)	1.12 (0.74 to 1.71)
Not acutely ill (n=850)				
2000–2004	27.0	9.4	—	—
2005–2009	30.6	17.0	1.28 (0.92 to 1.76)	2.02 (1.29 to 3.18)
Gastrointestinal signs and/or symptoms (n=860)				
2000–2004	26.7	8.1	—	—
2005–2009	25.2	15.6	0.97 (0.69 to 1.35)	2.06 (1.29 to 3.28)
Cardiopulmonary signs and/or symptoms (n=823)				
2000–2004	22.9	15.2	—	—
2005–2009	33.4	17.8	1.67 (1.19 to 2.34)	1.28 (0.85 to 1.93)
Fatigue and/or weakness (n=640)				
2000–2004	26.8	7.3	—	—
2005–2009	29.1	19.8	1.32 (0.90 to 1.92)	3.28 (1.91 to 5.64)
Electrolyte abnormalities (n=307)				
2000–2004	16.6	11.3	—	—
2005–2009	26.9	12.2	1.70 (0.89 to 3.24)	1.15 (0.53 to 2.50)
Neurologic signs and/or symptoms (n=281)				
2000–2004	20.0	14.1	—	—
2005–2009	28.1	16.4	1.52 (0.80 to 2.88)	1.04 (0.48 to 2.22)
Other signs and/or symptoms (n=357)				
2000–2004	17.7	10.3	—	—
2005–2009	31.9	14.8	2.31 (1.30 to 4.13)	1.64 (0.78 to 3.44)

<sup>a</sup>Referent eGFR<10 ml/min per 1.73 m<sup>2</sup>. Adjusted for age, race, sex, diagnoses of diabetes, congestive heart failure, ischemic heart disease, peripheral arterial disease, stroke, chronic obstructive pulmonary disease, risk score, eGFR slope during the year before initiation, site of initiation (inpatient versus outpatient), type of access at initiation (peritoneal dialysis catheter, hemodialysis graft or fistula, or hemodialysis catheter), and number of VA nephrology outpatient visits during the year before initiation.

<sup>b</sup>Adjusted analyses among all patients are additionally adjusted for whether the patient was acutely ill and signs and/or symptoms documented at the time of initiation.

in patients with protein energy malnutrition.<sup>15,16</sup> By 2006, KDOQI was suggesting that “particular clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy before stage 5.”<sup>17–19</sup> In addition to traditional indications, such as intractable volume overload, hyperkalemia, and pericarditis, this list also included relatively nonspecific signs and symptoms, such as “unexplained decline in functioning or well-being” and “weight loss or other evidence of malnutrition.”<sup>17–19</sup> This more liberal approach to dialysis initiation at higher levels of eGFR was facilitated by active collaboration between KDOQI and the Health Care Financing Administration to eliminate restrictions on the upper limit of renal function at which dialysis could be initiated without triggering a renal network review.<sup>16</sup>

Most members of this real-world cohort of patients initiating maintenance dialysis had documented signs and/or symptoms consistent with advanced kidney disease at the time of initiation. These are precisely the patients for whom the

relative benefits and harms of the observed trend toward earlier initiation of dialysis at higher levels of eGFR are not known. Many uremic signs and symptoms are common and relatively nonspecific (e.g., fatigue, nausea, malaise, and weakness), often leading to uncertainty in the clinical setting about etiology and the likely effect of dialysis. Observational data showing that symptom burden and quality of life are similar among patients with advanced kidney disease who are and are not treated with dialysis have highlighted a critical knowledge gap about the effect of dialysis on symptom burden.<sup>20–22</sup> Although alternative treatments (e.g., diuretics, low-protein diet, anion binding resins, and antiemetics) and approaches to care (e.g., palliative care) do exist, available trial data do not address the effectiveness of these alternatives compared (or combined) with dialysis in symptomatic patients, including the effect on symptom burden.<sup>6,23</sup> The Initiating Dialysis Early and Late (IDEAL) trial showed that delaying initiation until lower levels of eGFR in patients followed closely by a nephrologist did not result in

higher mortality, worse quality of life, or other adverse clinical outcomes.<sup>24,25</sup> However, more than one in three patients randomized to the late start arm of the IDEAL trial initiated dialysis before reaching their target eGFR. Uremic symptoms were cited as a reason for initiation in more than one half of these patients. A smaller trial of dialysis versus a very low-protein diet in adults older than 70 resulted in similar mortality and lower hospitalization rates for patients in the diet compared with dialysis arm.<sup>26</sup> Patients randomized to the diet arm started dialysis a median of 9 months after enrollment, mostly because of volume overload or hyperkalemia. However, the trial excluded patients with uremic signs and symptoms at baseline. More evidence on the benefits and harms of dialysis versus alternative approaches to the care of symptomatic patients with advanced kidney disease is needed to support discussions with patients and their families about whether and when to initiate dialysis.

Our study has the following limitations. First, the study was restricted to patients for whom the decision to initiate dialysis was made within the VA. Thus, it is possible that our results may not be generalizable to other practice settings and populations. Second, a total of 859 patients included in the chart review sample initiated dialysis outside the VA. Because level of acuity may influence whether decisions about dialysis initiation are made within the VA (e.g., urgent presentation to a non-VA hospital), our study may underestimate the percentage of patients within the VA who are acutely ill at the time of initiation. Third, although inclusion of information on clinical presentation at the time of initiation represents an important strength of this study, these analyses do not account for clinical signs and/or symptoms that were not documented in the electronic medical record. However, we found that decisions about dialysis initiation were generally quite well documented, and it is reassuring that one or more signs and/or symptoms were documented in the electronic record for the majority of patients included in the analytic sample. Fourth, the relatively small sample size limited the precision of estimates of trends in eGFR at initiation in stratified analyses.

An upward trend in eGFR at dialysis initiation within the VA health care system from 2000 to 2009 seems to reflect changes in the timing of dialysis initiation among patients with similar indications rather than changing indications over time.

## CONCISE METHODS

### Cohort

Our goal was to identify a cohort of patients within the VA who initiated dialysis over a 10-year period from FY 2000 to FY 2009 and for whom the decision to initiate dialysis was made within the VA. First, we designed a procedure code search of VA inpatient and outpatient administrative and fee basis files (that record care outside the VA that is paid for by the VA) to identify a denominator population that was receiving maintenance dialysis within or paid for by the VA during this time frame. Operationally, we defined maintenance dialysis as having a

procedure code for hemodialysis recorded on 15 separate days over a 60-day window or a single procedure code for peritoneal dialysis within the ascertainment period. This step yielded a cohort of 18,739 potentially eligible patients.

Second, we conducted a detailed medical record review among a random sample of these patients to identify a subset who met study inclusion criteria. For feasibility purposes, medical record review was restricted to a random sample of 3000 patients stratified by year of dialysis initiation. After reviewing the electronic medical records of these patients, we excluded 49 patients because they had not received maintenance dialysis during the observation period, 190 patients because the actual date of first dialysis documented in the electronic medical record occurred outside the observation period, 859 patients because the decision to initiate dialysis occurred outside the VA, 132 patients because a serum creatinine measurement within 45 days before dialysis initiation was not available in national VA sources, and 79 patients because the electronic medical record did not include adequate documentation of clinical presentation at the time of dialysis initiation. The remaining 1691 patients comprised the analytic cohort for this study. Compared with those excluded, patients in the analytic cohort were older (mean age=62.7±1.3 versus 60.9±11.6 years;  $P<0.001$ ) but had similar median risk scores and a similar gender and racial composition.

### Data Sources

Patient demographic and clinical characteristics were ascertained from a variety of different sources, including the VA enrollment file, Vital Status file, inpatient and outpatient treatment files, Decision Support System (DSS), and system-wide electronic medical record (VistAWeb) combined with Medicare inpatient and outpatient claims. Comorbid conditions were ascertained using diagnostic and procedure codes from both VA and Medicare inpatient and outpatient administrative data over the 1-year period before initiation. Information on serum creatinine measures before dialysis initiation and during the preceding 1-year period was ascertained from the VA DSS Laboratory Results (LAR) file. Date of death was ascertained from the VA Vital Status file. We used VistAWeb to access clinician notes (including those from physicians, nurses, and social workers) around the time of initiation to ascertain the true date of first dialysis, whether patients were acutely ill at the time of initiation, signs and/or symptoms documented around the time of initiation, dialysis modality and access used at the first dialysis session, and whether the patient initiated dialysis in the hospital. We used outpatient VA administrative data and Medicare claims to ascertain the number of outpatient nephrology visits within the VA during the year before initiation.

### Chart Abstraction

First, B.W. (a physician assistant and trained chart abstractor) reviewed the electronic medical record of all 3000 patients to identify a subset potentially eligible for study inclusion and ascertain the date of first dialysis, dialysis modality, and type of access at the time of initiation. This step yielded a total of 1735 patients potentially eligible for inclusion. Second, A.M.O. (a practicing nephrologist with more than a decade of clinical experience caring for patients with kidney disease) reviewed the electronic medical records of these patients to

confirm cohort eligibility and ascertain each patient's clinical presentation at the time of initiation. An additional 44 patients who did not meet cohort entry criteria were excluded in this step, yielding an analytic cohort of 1691 patients.

We used an inductive approach to characterize clinical presentation at the time of initiation on the basis of common themes identified in the electronic medical record of cohort patients. We developed classifications to characterize both overall clinical presentation and the types of clinical signs and/or symptoms documented in the electronic medical record around the time of initiation. Overall clinical presentation was characterized as whether the patient appeared to be acutely ill at the time of initiation. Patients were considered to be acutely ill if they started dialysis during a hospital admission for sudden worsening in their clinical status, regardless of whether the acute illness was directly related to their kidney disease or whether the acute symptoms had resolved at the time of dialysis initiation (Supplemental Table 1). Patients who were electively admitted to the hospital for the sole purpose of initiating dialysis were not classified as acutely ill unless they became acutely ill before dialysis initiation. For some patients, the decision to initiate dialysis seemed to be based primarily on their level of estimated kidney function, and signs and/or symptoms of advanced kidney disease were not documented or noted to be absent.

Documented signs and/or symptoms were grouped as follows: gastrointestinal, cardiopulmonary, fatigue and/or weakness, electrolyte abnormalities, neurologic (including difficulty sleeping), and other (including bleeding, hiccups, pruritis, and mention of uremia or uremic symptoms without additional specification). Patients could have symptoms falling within more than one of these groups. Supplemental Table 1 illustrates how notes from the electronic medical record were used to construct variables describing patients' clinical presentation at the time of dialysis initiation.

To assess the precision of ascertainment of illness acuity and clinical signs and symptoms from the electronic medical record by A.M.O., S.P.W. and M.K.Y. (senior fellows in nephrology) independently reviewed the electronic medical records of a random sample of 50 cohort members. Percentage of agreement with A.M.O. ranged from 76% to 92% across items (Supplemental Table 2). The  $\kappa$ -statistic ranged from 0.51 (signifying moderate agreement among the three expert reviewers) to 0.82 (signifying near perfect agreement) across items.<sup>27</sup>

To understand each patient's clinical presentation, we started by reviewing notes from nephrologists and nephrology fellows entered around the time of initiation. We then reviewed progress notes from other providers around this time as needed to fully characterize clinical presentation. In some instances, the decision to initiate dialysis was made weeks or months before dialysis was actually initiated. In these situations, we also looked back to earlier notes to ensure that we fully understood the clinical context of dialysis initiation. For patients who were not acutely ill at the time of initiation, renal clinic notes leading up to dialysis initiation usually provided most of the needed information. For patients who initiated dialysis in the setting of an acute illness, inpatient nephrology notes around the time of initiation, initial inpatient nephrology consult notes, admission history and physical examination notes, and discharge summaries were usually most informative.

### Level of eGFR at Initiation

Level of GFR at initiation was estimated on the basis of each patient's most recent serum creatinine measurement recorded in the VA DSS LAR file between 1 and 45 days before dialysis initiation. A small number of patients did not have a measurement during this time-frame but did have a measurement on the day of initiation, in which case we used that measurement. We used the Modification of Diet in Renal Disease equation to estimate GFR on the basis of age, race, gender and serum creatinine.

### Covariates

Covariates included race (white or nonwhite), comorbid conditions present during the 1-year period before initiation (diabetes, hypertension, coronary artery disease, cerebrovascular disease, peripheral arterial disease, congestive heart failure, and chronic obstructive pulmonary disease), and a Diagnostic Cost Groups case mix adjustment measure<sup>28</sup> (risk score) constructed by incorporating inpatient and outpatient diagnoses over the 1-year period before initiation from both VA and Medicare. We also included information on whether dialysis was initiated in the hospital, the number of VA outpatient nephrology visits during the 1-year period before initiation, and access used at first dialysis (peritoneal dialysis catheter, arteriovenous fistula, arteriovenous graft, or hemodialysis catheter). We used a mixed model to estimate eGFR slope for each patient using all inpatient and outpatient serum creatinine measurements from the DSS LAR file during the 1-year period before initiation.

### Analyses

We used chi-squared, *t*, and Mann–Whitney *U* tests as appropriate to compare the characteristics of patients who initiated dialysis in FYs 2000–2004 with those of patients who initiated dialysis in FYs 2005–2009. We used logistic regression analysis to examine the association between time period of dialysis initiation (FYs 2005–2009 versus FYs 2000–2004) and level of eGFR at initiation (categorized as <10 [reference], 10–15, and >15 ml/min per 1.73 m<sup>2</sup>). Multivariate analyses were adjusted for baseline patient characteristics at the time of initiation, documented clinical signs and/or symptoms, and whether the patient was acutely ill at the time of initiation. Multivariate analyses were repeated after stratification by level of acuity and types of documented signs and/or symptoms at the time of dialysis initiation. This research was approved by the Institutional Review Board at the VA Puget Sound Healthcare System.

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## DISCLOSURES

A.M.O. received royalties from UpToDate.

## REFERENCES

- Rosansky SJ, Clark WF, Eggers P, Glasscock RJ: Initiation of dialysis at higher GFRs: Is the apparent rising tide of early dialysis harmful or helpful? *Kidney Int* 76: 257–261, 2009
- Clark WF, Na Y, Rosansky SJ, Sontrop JM, Macnab JJ, Glasscock RJ, Eggers PW, Jackson K, Moist L: Association between estimated glomerular filtration rate at initiation of dialysis and mortality. *CMAJ* 183: 47–53, 2011
- O'Hare AM, Choi AI, Boscardin WJ, Clinton WL, Zawadzki I, Hebert PL, Kurella Tamura M, Taylor L, Larson EB: Trends in timing of initiation of chronic dialysis in the United States. *Arch Intern Med* 171: 1663–1669, 2011
- Kurella M, Covinsky KE, Collins AJ, Chertow GM: Octogenarians and nonagenarians starting dialysis in the United States. *Ann Intern Med* 146: 177–183, 2007
- Couchoud C, Guihenneuc C, Bayer F, Stengel B; REIN Registry: The timing of dialysis initiation affects the incidence of renal replacement therapy. *Nephrol Dial Transplant* 25: 1576–1578, 2010
- Abra G, Kurella Tamura M: Timing of initiation of dialysis: Time for a new direction? *Curr Opin Nephrol Hypertens* 21: 329–333, 2012
- Sood MM, Komenda P, Rigatto C, Hiebert B, Tangri N: The association of eGFR reporting with the timing of dialysis initiation. *J Am Soc Nephrol* 25: 2097–2104, 2014
- Lassalle M, Labeeuw M, Frimat L, Villar E, Joyeux V, Couchoud C, Stengel B: Age and comorbidity may explain the paradoxical association of an early dialysis start with poor survival. *Kidney Int* 77: 700–707, 2010
- Bao Y, Dalrymple L, Chertow GM, Kaysen GA, Johansen KL: Frailty, dialysis initiation, and mortality in end-stage renal disease. *Arch Intern Med* 172: 1071–1077, 2012
- O'Hare AM, Vig EK, Hebert PL: Initiation of dialysis at higher levels of estimated GFR and subsequent withdrawal. *Clin J Am Soc Nephrol* 8: 179–181, 2013
- Wong SP, Kreuter W, O'Hare AM: Healthcare intensity at initiation of chronic dialysis among older adults. *J Am Soc Nephrol* 25: 143–149, 2014
- Rosansky SJ: The sad truth about early initiation of dialysis in elderly patients. *JAMA* 307: 1919–1920, 2012
- Rosansky SJ, Eggers P, Jackson K, Glasscock R, Clark WF: Early start of hemodialysis may be harmful. *Arch Intern Med* 171: 396–403, 2011
- No authors listed: NKF-DOQI clinical practice guidelines for peritoneal dialysis adequacy. *Am J Kidney Dis* 30[Suppl 2]: S67–S136, 1997
- No authors listed: I. NKF-K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy: Update 2000. *Am J Kidney Dis* 37[Suppl 1]: S1–S64, 2001
- No authors listed: II. NKF-K/DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy: Update 2000. *Am J Kidney Dis* 37[Suppl 1]: S65–S136, 2001
- No authors listed: Clinical practice recommendations for peritoneal dialysis adequacy. *Am J Kidney Dis* 48[Suppl 1]: S130–S158, 2006
- Peritoneal Dialysis Adequacy 2006 Work Group: Clinical practice guidelines for peritoneal adequacy, update 2006. *Am J Kidney Dis* 48 [Suppl 1]: S91–S97, 2006
- Hemodialysis Adequacy 2006 Work Group: Clinical practice guidelines for hemodialysis adequacy, update 2006. *Am J Kidney Dis* 48[Suppl 1]: S2–S90, 2006
- Abdel-Kader K, Unruh ML, Weisbord SD: Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. *Clin J Am Soc Nephrol* 4: 1057–1064, 2009
- Murtagh FE, Addington-Hall J, Higginson IJ: The prevalence of symptoms in end-stage renal disease: A systematic review. *Adv Chronic Kidney Dis* 14: 82–99, 2007
- 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* 7: 2002–2009, 2012
- Rivara MB, Mehrotra R: Is early initiation of dialysis harmful? *Semin Dial* 27: 250–252, 2014
- Cooper BA, Branley P, Bulfone L, Collins JF, Craig JC, Fraenkel MB, Harris A, Johnson DW, Kesselhut J, Li JJ, Luxton G, Pilmore A, Tiller DJ, Harris DC, Pollock CA; IDEAL Study: A randomized, controlled trial of early versus late initiation of dialysis. *N Engl J Med* 363: 609–619, 2010
- Harris A, Cooper BA, Li JJ, Bulfone L, Branley P, Collins JF, Craig JC, Fraenkel MB, Johnson DW, Kesselhut J, Luxton G, Pilmore A, Rosevear M, Tiller DJ, Pollock CA, Harris DC: Cost-effectiveness of initiating dialysis early: A randomized controlled trial. *Am J Kidney Dis* 57: 707–715, 2011
- Brunori G, Viola BF, Parrinello G, De Biase V, Como G, Franco V, Garibotto G, Zubani R, Cancarini GC: Efficacy and safety of a very-low-protein diet when postponing dialysis in the elderly: A prospective randomized multicenter controlled study. *Am J Kidney Dis* 49: 569–580, 2007
- Viera AJ, Garrett JM: Understanding interobserver agreement: The kappa statistic. *Fam Med* 37: 360–363, 2005
- Maciejewski ML, Liu CF, Derleth A, McDonnell M, Anderson S, Fihn SD: The performance of administrative and self-reported measures for risk adjustment of Veterans Affairs expenditures. *Health Serv Res* 40: 887–904, 2005

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