Predictors of Timing of Dialysis Start in the United States

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USRDS Coordinating Center
USRDS Symposium, ASN 2014
Dialysis start is a time of high mortality risk, disruption to patients’ lives, and cost.

In this context, the decision about when to start dialysis (‘timing of start’) has tremendous implications for our patients.
Timing of Dialysis Start: Outline

• Trends in US
• Predictors (new analysis)
‘Timing’ of dialysis start  
(eGFR at start)

• In US, eGFR at dialysis start has been rising over time

• Attributed in part to 1997 KDOQI recommendation to start at GFR <10.5 ml/min/1.73m² (or <15 in some diabetics)

• Some practitioners undoubtedly have based decision to start dialysis on these eGFR cut points alone
Increase over time in eGFR at dialysis start

MDRD eGFR ml/min/1.73m²
Increase over time in eGFR at dialysis start

Percent starting dialysis at eGFR ≥10 ml/min/1.73m²
eGFR at start is higher in U.S. than other countries

eGFR immediately before dialysis

N Pts = mean =  
Bel 227 11.7 
Ger 346 11.2 
US 526 10.9 
Can 218 10.9 
Fra 89 8.4 
Spa 319 8.9 
UK 197 8.5 
ANZ 90 9.1 
Ita 202 8.3 
Swe 286 7.8 
Jpn 446 7.7 
Rus 70 7.1 
Chi 120 7.3 
GCC 145 6.2
eGFR at start is higher in U.S. than other countries

eGFR immediately before dialysis

DOPPS data; GFR at dialysis start, by country (2009-2014); Vintage ≤ 120 days
eGFR at dialysis start and clinical outcomes

• Evidence now indicates that early dialysis initiation does not prolong survival:
  – IDEAL, a multicenter clinical trial randomizing to start at CG GFR 10-14 vs. 5-7 mL/min/1.73 m²
  – Multiple observational studies
eGFR at dialysis start is leveling off

USRDS Annual Data Report, 2014
(unadjusted eGFR calculated with CKD-EPI equation)
Determinants of eGFR at Dialysis Start
Determinants of eGFR at Dialysis Start

Trends in Timing of Dialysis Initiation in the U.S. and Associations with Clinical and Non-Clinical Factors

Y Li, Y Jin, A Kapke, J Pearson, R Saran, F Port, B Robinson

(Manuscript in development)
Determinants of eGFR at Dialysis Start: 

Motivation for study

• It is likely some patients have initiated dialysis unnecessarily early
• This is concerning, particularly given our heightened awareness about the importance of patient-centered (individualized) care
• We set out to gain better understanding of the factors associated with the timing of dialysis initiation
Determinants of eGFR at Dialysis Start: 

*Prior Studies*

- Prior studies have:
  - Linked patient and provider characteristics to eGFR levels, but were cross-sectional in design, or
  - Focused on trends of eGFR at dialysis initiation, but were descriptive and lacked thorough covariate adjustments

Here, we examine factors associated with trends in eGFR over 18 years, using USRDS ESRD data from 1995 to 2012
Determinants of eGFR at Dialysis Start: 

*Research questions*

• Which patient, provider, and contextual factors are associated with (i) eGFR levels and (ii) trends over time in eGFR levels at dialysis initiation?

• How well do these factors explain the variation in eGFR levels at dialysis initiation?
Determinants of eGFR at Dialysis Start: Study hypotheses

1. eGFR at dialysis start is associated with clinical factors, but also non-clinical factors that are generally distinct from patient-centered care:
   – e.g., positive associations with male sex, white race, private insurance

2. There is large unexplained variation in eGFR at dialysis start
   – i.e., our available data are not sufficient to understand decisions regarding timing of dialysis initiation
Determinants of eGFR at Dialysis Start:  
*Methods*

• Data
  – USRDS data from 1995-2012
  – County-level data from the 2000 US Census
  – eGFR level was calculated via four-variable MDRD (age, serum creatinine, gender, and race), based on Form 2728

• Analysis
  – Linear mixed model on eGFR
  – Accounted for physician clusters
  – Adjusted for year and patient-level, facility-level, county-level variables
  – Time interaction terms
Temporal trends in eGFR* at dialysis start:  
*Distribution by year (1995-2012)*

![Graph showing temporal trends in eGFR at dialysis start]

<table>
<thead>
<tr>
<th>Year</th>
<th>1995</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>7.7</td>
<td>10.9</td>
</tr>
<tr>
<td>median</td>
<td>7.0</td>
<td>10.4</td>
</tr>
<tr>
<td>10th</td>
<td>4.1</td>
<td>5.3</td>
</tr>
<tr>
<td>90th</td>
<td>12.2</td>
<td>17.9</td>
</tr>
</tbody>
</table>

* *eGFR with values <2 were set to 2 and with values >20 were set to 20.*

Data source: USRDS ESRD database
Temporal Trends in eGFR at Dialysis Start by Demographics

### Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Difference in Mean eGFR</th>
<th>Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>[18, 45]</td>
<td>-0.89</td>
<td>-0.59</td>
</tr>
<tr>
<td>[45, 65]</td>
<td>-0.68</td>
<td>-0.39</td>
</tr>
<tr>
<td>≥65</td>
<td>REF</td>
<td>REF</td>
</tr>
</tbody>
</table>

### Sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>Difference in Mean eGFR</th>
<th>Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1.03</td>
<td>-0.02 (NS)</td>
</tr>
<tr>
<td>Female</td>
<td>REF</td>
<td>REF</td>
</tr>
</tbody>
</table>

Analysis used a linear mixed model, adjusted for designated variables and with an interaction term for time and the variable of interest.

Data source: USRDS ESRD database
Temporal Trends in eGFR at Dialysis Start by Comorbidities

**Diabetes**

<table>
<thead>
<tr>
<th>Difference in Mean eGFR</th>
<th>Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>1.16</td>
</tr>
<tr>
<td>No Diabetes</td>
<td>REF</td>
</tr>
</tbody>
</table>

**Heart Disease**

<table>
<thead>
<tr>
<th>Difference in Mean eGFR</th>
<th>Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>1.59</td>
</tr>
<tr>
<td>ASHD, Stroke or PVD</td>
<td>0.58</td>
</tr>
<tr>
<td>No Heart Disease</td>
<td>REF</td>
</tr>
</tbody>
</table>

Analysis used a linear mixed model, adjusted for designated variables and with an interaction term for time and the variable of interest.

Data source: USRDS ESRD database
Temporal Trends in eGFR at Dialysis Start by Socioeconomic Factors

### Employment Status

<table>
<thead>
<tr>
<th>Employment Status</th>
<th>Difference in Mean eGFR</th>
<th>Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employed</td>
<td>-0.77</td>
<td>-0.28</td>
</tr>
<tr>
<td>Unemployed</td>
<td>REF</td>
<td>REF</td>
</tr>
</tbody>
</table>

### Insurance Status

<table>
<thead>
<tr>
<th>Insurance Status</th>
<th>Difference in Mean eGFR</th>
<th>Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Insurance</td>
<td>-0.81</td>
<td>-0.42</td>
</tr>
<tr>
<td>Insurance</td>
<td>REF</td>
<td>REF</td>
</tr>
</tbody>
</table>

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Data source: USRDS ESRD database
Temporal Trends in eGFR at Dialysis Start by Treatment Variables

### Catheter Use

<table>
<thead>
<tr>
<th>Difference in Mean Increase in eGFR</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Catheter Use</strong></td>
<td>-0.19</td>
<td>-0.03 (NS)</td>
</tr>
<tr>
<td>No</td>
<td>REF</td>
<td>REF</td>
</tr>
</tbody>
</table>

### Prior Nephrology Care

<table>
<thead>
<tr>
<th>Difference in Mean Increase in eGFR</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prior Nephrology Care</strong></td>
<td>0.31</td>
<td>0.12</td>
</tr>
<tr>
<td>No</td>
<td>REF</td>
<td>REF</td>
</tr>
</tbody>
</table>

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Data source: USRDS ESRD database
Temporal Trends in eGFR at Dialysis Start by Facility Characteristics

Profit Status

<table>
<thead>
<tr>
<th>Profit Status</th>
<th>Difference in Mean eGFR Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-profit</td>
<td>-0.06</td>
</tr>
<tr>
<td>Profit</td>
<td>REF</td>
</tr>
</tbody>
</table>

Facility Size

<table>
<thead>
<tr>
<th>Facility Size</th>
<th>Difference in Mean eGFR Increase in eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>0.08</td>
</tr>
<tr>
<td>No</td>
<td>REF</td>
</tr>
</tbody>
</table>

Analysis used a linear mixed model, adjusted for designated variables and with an interaction term for time and the variable of interest.

Data source: USRDS ESRD database
Change of eGFR at dialysis start: By ESRD Network

Adjusted difference in eGFR increase from 1995-2009, compared to average

-0.63 to -0.26
-0.25 to -0.07
-0.04 to 0.21
0.27 to 0.65

Data source: USRDS ESRD database, 1995-2009
**eGFR at Dialysis Start: Proportion of Variance Explained**

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmeasured factors and random error</td>
<td>75.6%</td>
</tr>
<tr>
<td>Explained by model</td>
<td>24.4%</td>
</tr>
<tr>
<td>Total variance in eGFR (100%)</td>
<td></td>
</tr>
<tr>
<td>Variance explained by model (24.4%)</td>
<td></td>
</tr>
<tr>
<td>Calendar year</td>
<td>5.1%</td>
</tr>
<tr>
<td>Unmeasured physician-level Factors</td>
<td>6.6%</td>
</tr>
<tr>
<td>Interaction terms with year</td>
<td>0.2%</td>
</tr>
<tr>
<td>Facility or county-level factors</td>
<td>0.9%</td>
</tr>
<tr>
<td>Patient-level factors</td>
<td>11.6%</td>
</tr>
<tr>
<td>Other factors and random errors</td>
<td>75.6%</td>
</tr>
</tbody>
</table>

*These proportions of variation explained were only minimally affected by the order of sets of variables that entered the linear mixed model, which is reflected by the small ranges of these proportions.*

Data source: USRDS ESRD database, 1995-2009
eGFR at Dialysis Start: Proportion of Variance Explained*

*These proportions of variation explained were only minimally affected by the order of sets of variables that entered the linear mixed model, which is reflected by the small ranges of these proportions.

Data source: USRDS ESRD database, 1995-2009
Unexplained Variation: Factors that influence ‘timing’ of start of dialysis (beyond eGFR)

• Rate of change in eGFR
• Underlying health: Frailty, comorbidities
• Complications of uremia: worsening nutrition, uremic symptoms, hyperkalemia
• Mature / maturing vascular access
• Patient preference / social support
• Others
Temporal Trends in eGFR at Dialysis Start: Summary (1)

• The year-after-year trend in rising eGFR at dialysis start has now leveled off!

• Nonetheless, the mean eGFR has risen by 3.2 ml/min/1.73m² since 1995

• Variation across patients (range in eGFR at start) is more substantial than average trends over time
Temporal Trends in eGFR at Dialysis Start: Summary (2)

• Higher average eGFR levels, and/or faster increase in eGFR, at start are associated with:
  – Clinical status: Older age and most comorbidities
  – Treatment factors: surgical vascular access, pre-dialysis nephrology care
  – Male sex and (among <65yr) private insurance, ESRD network; these may reflect potentially modifiable differences in access to care or intensity of care
Temporal Trends in eGFR at Dialysis Start: Summary (3)

*It’s not just about eGFR…*

- The finding that the majority of variation in eGFR at start is unexplained indicates that most patients aren’t started based on eGFR alone (this is good – suggests individualized care!)

- We need new studies to gain understanding of decisions surrounding dialysis initiation & implications for patients
Temporal Trends in eGFR at Dialysis Start: Summary (3)

*It’s not just about eGFR...*

- The finding that the majority of variation in eGFR at start is unexplained indicates that most patients aren’t started based on eGFR alone (this is good – suggests individualized care!)

- We need new studies to gain understanding of decisions surrounding dialysis initiation & implications for patients
  - Prospective cohort studies (e.g., EQUAL, CKDopps)
  - New USRDS Special Study (Dr. Kalantar-Zadeh)