Renal Replacement Therapy and Incremental Hemodialysis for Veterans with Advanced Chronic Kidney Disease


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ABSTRACT

Each year approximately 13,000 Veterans transition to maintenance dialysis, mostly in the traditional form of thrice-weekly hemodialysis from the start. Among >6000 dialysis units nationwide, there are currently approximately 70 Veterans Affairs (VA) dialysis centers. Given this number of VA dialysis centers and their limited capacity, only 10% of all incident dialysis Veterans initiate treatment in a VA center. Evidence suggests that, among Veterans, the receipt of care within the VA system is associated with favorable outcomes, potentially because of the enhanced access to healthcare resources. Data from the United States Renal Data System Special Study Center “Transition-of-Care-in-CKD” suggest that Veterans who receive dialysis in a VA unit exhibit greater survival compared with the non-VA centers. Substantial financial expenditures arise from the high volume of outsourced care and higher dialysis reimbursement paid by the VA than by Medicare to outsourced providers. Given the exceedingly high mortality and abrupt decline in residual kidney function (RKF) in the first dialysis year, it is possible that incremental transition to dialysis through an initial twice-weekly hemodialysis regimen might preserve RKF, prolong vascular access longevity, improve patients’ quality of life, and be a more patient-centered approach, more consistent with “personalized” dialysis. Broad implementation of incremental dialysis might also result in more Veterans receiving care within a VA dialysis unit. Controlled trials are needed to examine the safety and efficacy of incremental hemodialysis in Veterans and other populations; the administrative and health care as well as provider structure within the VA system would facilitate the performance of such trials.

Veterans Health Care in the United States

The term “Veterans” typically refers to persons who previously served in the armed services. According to the United States (US) government, a Veteran is defined as a person who served in the active military (army, naval, marine corps, air service, or coast guard) and who was discharged or released under conditions other than those that were
Veterans with Advanced CKD and ESRD

Each year 12,000–14,000 Veterans with advanced CKD, i.e., estimated glomerular filtration rate (eGFR) <25 ml/minute/1.73 m², transition to ESRD to receive renal replacement therapy, mostly in the form of maintenance dialysis treatment (see Table 1) (9). Hence, Veterans comprise 11% of the nation’s incident dialysis population, given that 110,000–120,000 persons initiate maintenance dialysis treatment each year in the US (9,10). Of the 450,000 US Americans who currently undergo maintenance dialysis treatment, approximately 35,000 or more are Veterans, reflecting a higher ESRD prevalence among Veterans than in the general US population (604 versus 187 per 100,000, respectively) (11). The majority of these patients undergo thrice-weekly hemodialysis from Day 1 of treatment. The vast majority of VA dialysis centers are based in VA hospitals, with the exception of a few off-campus dialysis units that have recently been established (12). Hence, the national VA dialysis system can be considered a quasi “medium dialysis organization” or chain with a somewhat more homogeneous practice pattern. Most of the VA hospital-based dialysis units provide both maintenance outpatient and acute inpatient dialysis treatments in the same location simultaneously, including dialysis treatment for Veterans with ESRD who are admitted to the hospital as well as those with acute kidney injury (AKI) requiring renal replacement therapy. To that end, a VA dialysis center is unique, as compared with other non-VA dialysis clinics where, until December 2016, inpatient dialysis treatments might not be performed according to the condition of coverage regulations governed by the Center for Medicare and Medicaid Services (CMS) (13).

The VHA provides comprehensive medical care for patients with kidney disease, including all stages of CKD as well as AKI. Any enrolled Veteran who develops ESRD is eligible to receive renal replacement therapy from the VHA. Dialysis care is a covered benefit under VA’s Medical Benefits Package for Veterans enrolled in the VA, irrespective of their service connectedness (13). For patients requiring in-center dialysis treatment, the VHA provides dialysis both through units maintained and operated by the individual VA facilities (hence usually hospital-based dialysis centers), or by outsourcing dialysis services to private dialysis providers. This may happen in cases where the distance from a VA facility is prohibitive for thrice-weekly dialysis therapy, when there is a lack of home dialysis resources or expertise, or when the capacity of the VA facility-operated dialysis unit is exceeded (13).

TABLE 1. Incidence and rates of end-stage renal disease (ESRD) among United States (US) Veterans, from 2008 to 2013, with comparison to the entire US population. Note that the denominators may not be commensurate given the older age of veterans. Note that the Veteran denominator may be inflated 2-fold given that less than half of all veterans are enrolled in the VHA. Adopted from the United States Renal Data System 2015/2016 Annual Data Report (9)

<table>
<thead>
<tr>
<th>Calendar year</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veterans with incident ESRD</td>
<td>13,529</td>
<td>13,842</td>
<td>13,448</td>
<td>12,755</td>
<td>12,869</td>
</tr>
<tr>
<td>All Veterans</td>
<td>22,424,712</td>
<td>21,854,374</td>
<td>21,798,077</td>
<td>21,458,427</td>
<td>21,230,865</td>
</tr>
<tr>
<td>Incidence rate of ESRD in Veterans, PM</td>
<td>2760</td>
<td>2874</td>
<td>2792</td>
<td>2680</td>
<td>2716</td>
</tr>
<tr>
<td>Incident ESRD in US</td>
<td>112,483</td>
<td>116,178</td>
<td>116,580</td>
<td>114,613</td>
<td>116,615</td>
</tr>
<tr>
<td>Adult US population</td>
<td>230,478,491</td>
<td>232,666,095</td>
<td>233,971,134</td>
<td>236,462,244</td>
<td>238,925,961</td>
</tr>
<tr>
<td>ESRD incidence rate in the US, PM</td>
<td>3992</td>
<td>4036</td>
<td>3992</td>
<td>3826</td>
<td>3772</td>
</tr>
</tbody>
</table>

PM, per million.
Given the relatively small number of VA-based dialysis centers in the nation and their limited capacity (each usually has only 10–20 dialysis stations), only 10% of all Veterans with advanced CKD initiate dialysis treatment in a VA dialysis center, while 90% initiate dialysis care in outside (non-VA) dialysis units, some under a subcontracted system. Recent data including reports from the United States Renal Data System (USRDS) (see below) suggest that Veterans who receive care within a VA dialysis center exhibit greater survival than those in non-VA dialysis units (9,10). Furthermore, substantial financial expenditures arise for outsourcing Veterans’ dialysis treatments in non-VA dialysis centers given higher dialysis reimbursement paid by the VA than by CMS to non-VA dialysis providers (11). Hence, there are compelling reasons to explore effective ways to expand access to and capacity within the VA dialysis programs to permit more Veterans with ESRD to receive care within the VA healthcare system.

**Transition of Veterans to Renal Replacement Therapy**

In 2014, a new USRDS Special Study Center under the designation “Transition-of-Care-in-CKD” (TC-CKD) was created to focus on examining patients who transition to renal replacement therapy, with special attention to risk factors in the pre-dialysis period. Among others, the TC-CKD Special Study Center has examined and annually reported the data on all Veterans who have transitioned to ESRD starting from the fiscal year 2007 and onwards. The initial TC-CKD reports included 52,172 Veterans who transitioned to ESRD over a 4-year period (10/1/2007–9/30/2011) (Table 2) (10). Within this cohort, 83% and 78% were assigned to in-center hemodialysis on Day 1 and Day 90 of treatment, respectively, while those receiving home hemodialysis remained at only 0.5%. Peritoneal dialysis comprised 5% of modalities. A total of 589 Veterans (1.1%) received pre-emptive kidney transplantation. Most notably, however, 5348 or 10% of the Veterans died in the first 90 days of dialysis treatment, translating into an equivalent annualized mortality of 41% for the first 3 months, while 1798 (3.5%) regained kidney function and stopped dialysis treatment, likely after resolution of presumed AKI (see Table 2). The high early dialysis mortality is also shown in Fig. 1 and discussed further (see below) (10).

Only 5157 of these 52,172 Veterans (9.9%) received dialysis therapy in a dialysis unit based in a VA Medical Center (Table 3); the majority (90%) were outsourced to private dialysis providers, including large for-profit dialysis organizations (27.6% and 24.5% of Veterans treated within Fresenius and DaVita dialysis units, respectively), other dialysis chains (13.1%), or an independent dialysis center (21.1%). After 3 months of treatment, among Veterans continuing to require renal replacement therapy for ESRD, 52.4% still received dialysis therapy in a for-profit large dialysis organization, 13.2% in other dialysis chains, 21.1% in independent (here referred to as “non-chain”) dialysis centers, 2.5% in non-specified (unknown) facilities, and 10.7% in the VA medical center-based dialysis units, suggesting that the dialysis provider proportions remain relatively constant over time.

Veterans who received dialysis treatment in a VA medical center were on average 5–7 years younger than the Veterans in a non-VA dialysis clinics, such that only 42.4% of the former patients were older than 65 years as compared with 64.8% of all Veterans with incident ESRD (Table 3). The VA Medical Centers had a higher prevalence of African Americans (42.6%) as compared with all Veterans with incident ESRD (25.9%). Dialysis patients who received treatment in a dialysis unit based in a VA hospital exhibited a greater survival at any given month over the first 24 months of dialysis initiation or vintage (Fig. 1). Furthermore, the high early mortality surge notable in the first several months of treatment across all dialysis providers is attenuated among those receiving care within VA dialysis units. Preliminary analyses show that this survival

### TABLE 2. Renal replacement therapy modalities on Days 1, 30, 60, and 90 of end-stage renal disease (ESRD) in 52,172 Veterans who transitioned to ESRD over a 4-year period (from 10/1/2007 through 9/30/2011). Adapted from the United States Renal Data System 2014/2015 Annual Data Report (10)

<table>
<thead>
<tr>
<th>Dialysis modality</th>
<th>Day 1</th>
<th>Day 30</th>
<th>Day 60</th>
<th>Day 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-center HD</td>
<td>43,242</td>
<td>43,244</td>
<td>43,149</td>
<td>40,905</td>
</tr>
<tr>
<td>Home HD</td>
<td>260 (0.5)</td>
<td>260 (0.5)</td>
<td>259 (0.5)</td>
<td>258 (0.5)</td>
</tr>
<tr>
<td>CAPD</td>
<td>1405 (2.7)</td>
<td>1405 (2.7)</td>
<td>1398 (2.7)</td>
<td>1302 (2.5)</td>
</tr>
<tr>
<td>CCPD</td>
<td>1165 (2.2)</td>
<td>1165 (2.2)</td>
<td>1173 (2.3)</td>
<td>1387 (2.7)</td>
</tr>
<tr>
<td>Other PD</td>
<td>9 (&lt;0.1)</td>
<td>9 (&lt;0.5)</td>
<td>9 (&lt;0.1)</td>
<td>8 (&lt;0.1)</td>
</tr>
<tr>
<td>Uncertain modality</td>
<td>5301 (10)</td>
<td>3509 (6.7)</td>
<td>626 (1.2)</td>
<td>460 (0.9)</td>
</tr>
<tr>
<td>Death</td>
<td>201 (0.4)</td>
<td>1561 (2.9)</td>
<td>3672 (7.1)</td>
<td>5348 (10.3)</td>
</tr>
<tr>
<td>Transplant</td>
<td>589 (1.1)</td>
<td>654 (1.3)</td>
<td>679 (1.3)</td>
<td>701 (1.3)</td>
</tr>
<tr>
<td>Loss to follow-up</td>
<td>n/a</td>
<td>3 (&lt;0.1)</td>
<td>3 (&lt;0.1)</td>
<td>5 (&lt;0.1)</td>
</tr>
<tr>
<td>Recovery of kidney function</td>
<td>n/a</td>
<td>362 (0.7)</td>
<td>1204 (2.3)</td>
<td>1798 (3.5)</td>
</tr>
<tr>
<td>Total N</td>
<td>52,172</td>
<td>52,172</td>
<td>52,172</td>
<td>52,172</td>
</tr>
</tbody>
</table>

HD, hemodialysis; PD, peritoneal dialysis; CAPD, chronic ambulatory peritoneal dialysis; CCPD, automated (continuous cycling) peritoneal dialysis.

Values in parenthesis are expressed in %.
superiority of the VA dialysis units persists even after multivariate adjustment for case-mix characteristics (14).

**Disparities Among Veterans with Incident ESRD Across the Nation**

The TC-CKD Special Study Center chapter in the 2016 USRDS Annual Data Report (15) highlights the characteristics of 85,505 Veterans with incident ESRD who transitioned to dialysis over the period of 10/1/2007–3/31/2014, i.e., over six-and-a-half years. The cohort’s mean ± SD age was 70.1 ± 12.0 years, and included patients among whom 25% were of Black race and 6% were of Hispanic ethnicity. The main causes of ESRD were diabetes mellitus (42%) or hypertension (31%). Across the nation, the proportion of Black Veterans with incident ESRD varied by state and region. Southern states, such as Alabama, Georgia, Louisiana, Mississippi, and Washington D.C. had the highest prevalences of Black Veterans who transitioned to ESRD, whereas northeastern and northwestern states had lower proportions (Fig. 2) (15).

The national rate of pre-emptive kidney transplantation among Veterans with advanced CKD over the same period is shown in Fig. 3 (15). The rates were calculated based on the number of pre-emptive transplants divided by the total number of Veterans with incident ESRD in that state or territory ($n = 1133$ pre-emptive transplantations over six-and-a-half years in the entire nation). The states with the highest pre-emptive kidney transplantation rates among Veterans ($>2.1\%$) were Alaska, Colorado, Delaware, Maryland, Minnesota, Montana, New Mexico, Utah, Vermont, and Wyoming. Juxta-positioning these two sets of figures highlight potential areas of disparity for pre-emptive kidney transplantation across race, implying that there are opportunities to more accurately identify and address the discrepancies related to renal replacement therapy modalities and distribution across Veterans throughout the nation.

A recent landmark study by Kovesdy et al. (4) showed that, by having equal access to healthcare resources in the VHA system, African Americans have lower all-cause mortality and incidence of coronary heart disease as well as a similar incidence of ischemic stroke, which stands in contrast to the higher mortality observed among Black individuals in the general US population outside of the VA system. Hence, Veterans’ increased opportunity to receive dialysis care within an integrated healthcare system could yield improved understanding of drivers of disparities in CKD care. In addition, leveraging the VHA’s considerable research infrastructure would permit the discovery of additional health service delivery innovations to reduce disparities and improve outcomes of people with ESRD.

**Incremental Dialysis Initiation for Veterans**

Whereas prevalent dialysis patients have an exceptionally high mortality rate of 15–20% per year nationwide, worse than most malignancies (16), mortality is even higher in the first several months of dialysis therapy with the annualized
mortality surpassing 40% as discussed above (see Fig. 1 and Table 3). Although a limited number of controlled trials have examined the extent to which clinical outcomes can be improved among the prevalent dialysis patients, interventions among incident dialysis patients have largely been overlooked.
despite their high mortality, morbidity, and marked decrements in health-related quality of life. There is an urgent need to address the exceptionally high death rate of incident dialysis patients. While reasons for high early mortality are likely complex, two potentially modifiable factors include: (1) loss of residual kidney function and (2) decline in health-related quality of life, both of which may be direct consequences of abrupt initiation of thrice-weekly hemodialysis treatment. It has been suggested, although not unequivocally proven, that thrice-weekly or more frequent hemodialysis upon transition to renal replacement therapy may accelerate loss of residual kidney function whereas a more gradual transition to dialysis, e.g., once to twice-weekly hemodialysis in the first several months of dialysis initiation, may preserve residual kidney function. Moreover, a less frequent initial hemodialysis schedule may make it easier for some patients to adapt to renal replacement therapy with less disruption and strain upon their lifestyles. Indeed, both of these factors—residual kidney function and elevated health-related quality of life—are among the two strongest predictors of survival in the first year of dialysis therapy (17).

Although not currently the standard of care in the US, there is increasing evidence to suggest that initiation of hemodialysis using a twice-weekly schedule may offer meaningful benefits, even if transition to thrice-weekly hemodialysis is later required (17–19). This incremental hemodialysis approach provides a more gradual and tolerable transition to renal replacement therapy, potentially resulting in better health-related quality of life, longer preservation of the residual kidney function (20,21), reduction of hemodialysis-induced inflammatory and oxidative stress (22), decreased frequency of intra-dialytic hypotension, reduced erythropoiesis-stimulating agent dose, and reduced morbidity and mortality (23,24). Most importantly, dialysis initiation with twice-weekly hemodialysis may support a more patient-centered approach, as it may improve quality of life by offering a more flexible approach to dialysis prescription. Having the option to dialyze twice rather than thrice weekly may improve quality of life for some patients. Potential benefits include fewer intrusions on day-to-day living, employment, and relationships; more limited exposure to post-dialysis fatigue; and lower costs. By offering an alternative to thrice weekly dialysis and an incremental approach to hemodialysis initiation, addition of twice weekly dialysis as a treatment option would help to support a more patient-centered approach to dialysis prescription that would make it easier to align therapy with patient goals and preferences.

Twice-weekly hemodialysis at the time of initiation builds upon the concept of “Incremental Dialysis” initially described among peritoneal dialysis patients. In patients who start with peritoneal dialysis, residual kidney function is often critical to solute clearance, fluid balance, and survival, and can be preserved by avoiding nephrotoxic agents and by pharmacotherapeutic modulation of the renin angiotensin aldosterone pathway (25). Although widely accepted as a treatment strategy among peritoneal dialysis patients, this strategy has tended not to be adopted in the provision of hemodialysis. The current US paradigm is to initiate “full-dose,” thrice-weekly hemodialysis therapy

### Figure 3

Distribution of pre-emptive kidney transplantation rates among 85,505 incident end-stage renal disease (ESRD) Veterans across states and territories of the United States over six-and-a-half years, i.e., 10/1/2007–3/31/2014 (adapted from Figure 8.3. in Vol 1 of the Transition of Care in Chronic Kidney Disease chapter of the 2016/2017 United States Renal Data System Annual Data Report) (15). This figure depicts states and territories of the United States. [Color figure can be viewed at wileyonlinelibrary.com]
without prescription adjustment irrespective of presence of residual kidney function and changes over time is extremely rigid and does not provide the kind of flexibility often needed in supporting the myriad goals and priorities of individual patients. If twice-weekly hemodialysis were to be widely available for incident Veterans with advanced CKD who are approaching ESRD, it would allow for expansion in dialysis capacity within the VA and more Veterans could receive care in VA-based dialysis units (Fig. 1 and Table 3). Evidence suggests that over half to two-thirds or more of new ESRD patients have adequate residual kidney function for initiation of incremental hemodialysis initiation. While there are many factors beyond RKF that determine the optimal frequency of dialysis for individual patients, the 2006 Kidney Disease Outcome Quality Initiative dialysis adequacy guidelines, a urea clearance (KRU) greater than 3 ml/minute/1.73 m$^2$ is sufficient for twice-weekly hemodialysis therapy, whereas a decline in KRU to below 2 ml/minute/1.73 m$^2$ is suggested as a transition point for increasing frequency to thrice-weekly treatment (26). From a system perspective, twice-weekly hemodialysis practice model would allow facilities to start three patients on treatment using the same resources as two patients on thrice-weekly hemodialysis (Fig. 4). According to our simulations, if each year 60% of the 12,000–13,000 Veterans starting thrice-weekly hemodialysis are instead initiated on twice-weekly hemodialysis, and assuming that the median time to the needed transition from twice-weekly to thrice-weekly HD is 9 months based on suggested criteria (Table 4), then each year 300–500 more Veterans could be accommodated within the VA system.

For widespread acceptance of incremental twice-weekly hemodialysis to be broadly implemented among Veterans, a pragmatic randomized-controlled trial across multiple VA dialysis centers is needed to support the safety, feasibility and acceptability of this approach. Such a trial could (27) examine the hypothesis that Veterans who initiate maintenance dialysis therapy and who have reasonable residual kidney function, e.g., >500 ml/day urine output and >3 ml/minute/1.73 m$^2$ urea clearance, twice-weekly hemodialysis during the first 12 months of dialysis therapy will be safe and effective and will result in preservation of residual kidney function and improved health-related quality of life without compromising survival. Other relevant endpoints to be examined would include reduction in inflammatory and oxidative stress, patient and dialysis staff satisfaction, dialysis vascular access longevity, and risk of hospitalization and readmission. The trial could also be designed to address several clinically related questions such as the roles of loop diuretics administration and avoidance of nephrotoxic agents in preserving residual kidney function longer.

How to Implement and Monitor Incremental Hemodialysis

In 2014, the blueprint of a Decision Support System for implementation and monitoring of incremental hemodialysis was developed by a group of experts in the setting of a consensus article (Box 1) (17). This Decision Support System was based on ten clinical metrics to guide the initial hemodialysis dose and frequency as well as the transition points for escalation from twice-weekly to thrice-weekly hemodialysis, and was tailored for dialysis practice in resource limited economies where KRU may not be readily available. In the current review paper, we
have added KRU (>3 ml/minute/1.73 m² to start twice-weekly hemodialysis and <2 ml/minute/1.73 m² to transition to thrice-weekly hemodialysis) as the 11th metric (see Box 1). These metrics should be re-examined in individual patients periodically (e.g., monthly to quarterly) to help guide the dose and frequency of hemodialysis treatment individually. RKF, including the modified urine volume criterion (>600 ml/day as the minimum urine output threshold to consider twice-weekly hemodialysis and <500 ml/day as the transition point for thrice-weekly hemodialysis) along with the above-mentioned KRU threshold levels, is perhaps the most important determinant of dialysis dose and frequency (17). The proposed modified Decision Support System criteria (Box 1) can be used to this end until the results of additional comparative effectiveness studies or randomized-controlled trials are available.

### How to Reconcile Incremental with Conventional and More Frequent Hemodialysis?

There is a general misconception that the objectives of incremental hemodialysis conflicts with conventional thrice-weekly and more frequent hemodialysis regimens. Indeed, the incremental hemodialysis approach is based on the premise that many patients who have initiated renal replacement therapy with a twice-weekly regimen will eventually benefit from transitioning to thrice-weekly and more frequent hemodialysis schedules given the inevitable decline in residual kidney function with the passage of time among most ESRD patients. Hence, incremental hemodialysis offers an opportunity to expand the spectrum of dialysis frequency (leftward on Fig. 5) and to support a more individualized or personalized approach to dialysis prescription.

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**Box 1** Proposed Decision Support System with 11 criteria for initiating and maintaining incremental (twice-weekly) hemodialysis (HD) treatment upon transition to end-stage renal disease (adapted from Kalantar-Zadeh et al. (17) and Rhee et al. (33))

### Incremental (twice-weekly) hemodialysis treatment criteria

1. Adequate residual kidney function with urine output > 600 ml/day (transition to thrice-weekly if urine output drops to < 500 ml/day)
2. Limited fluid retention between two consecutive HD treatments with a fluid gain < 2.5 kg (or less than 5% of the ideal dry weight) without HD for 3–4 days
3. Limited or readily manageable cardiovascular or pulmonary symptoms without clinically significant fluid overload
4. Suitable body size relative to residual renal function; patients with larger body size may be suitable for twice-weekly hemodialysis if not hypercatabolic
5. Hyperkalemia (K > 5.5 mEq/l) infrequent or readily manageable
6. Hyperphosphatemia (P > 5.5 mg/dl) infrequent or readily manageable
7. Good nutritional status without florid hypercatabolic state
8. Lack of profound anemia (hemoglobin > 8 g/dl) and appropriate responsiveness to anemia therapy
9. Infrequent hospitalization and easily manageable comorbid conditions
10. Satisfactory health-related quality of life and functional status
11. Residual urea clearance (KRU) > 3 ml/minute/1.73m² (transition to thrice-weekly if KRU < 2 ml/minute/1.73m²)

### Implementation strategies

1. To initiate twice-weekly hemodialysis, the patient should meet the first (urine output > 600 ml/day) and the last criteria (KRU > 3 ml/minute/1.73m²), plus most (five out of nine) other criteria
2. Examine these criteria every 1–3 months in all twice-weekly hemodialysis patients and compare outcome measures between twice-weekly and thrice-weekly hemodialysis patients to assure outcome non-inferiority for continuation of twice-weekly hemodialysis
3. Consider transition from a twice-weekly to thrice-weekly hemodialysis regimen if patient’s urine output drops < 500 ml/day, if KRU declines < 2 ml/minute/1.73m², or if patient’s nutritional status or general health condition shows a deteriorating trend over time

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*a The proposed criteria may be refined for use in clinical trials and clinical decision making.

*b The minimum required urine output to initiate twice-weekly has been changed to 600 ml/day in this adaptation, while >500 ml/day is needed to maintain twice-weekly regimen.

*c Lack of systolic dysfunction (EF > 40%) and no major coronary intervention over the past 3 months.

*d Criterion #11 in this adaptation.
Traditional and novel urea kinetics models with more accurate incorporation of RRF can be employed or developed and evolved to more effectively explore as to how incremental versus conventional hemodialysis regimens can be evaluated for commensurate urea clearance (28). Given recent data suggesting limited reduction in uremic solute concentrations with increased dialysis frequency and time in the Frequent Hemodialysis Network Daily Trial (29), more clearance may not necessarily equate with more effective uremia management (30). To date, there have been no controlled trials of incident ESRD patients transitioning to hemodialysis based on the collective of urea kinetics of the dialysis therapy and residual kidney function combined.

**Veterans’ Preference of Dialysis Treatment**

According to some of the coauthors of this and other articles (17) who serve as VA staff nephrologists, clinicians caring for Veterans with ESRD often encounter patients who prefer to receive hemodialysis less frequently than the currently recommended thrice-weekly protocol. The option of a less intensive treatment regimen may be particularly valuable for patients who are transitioning to dialysis, approaching the end of life and/or have competing priorities that make it difficult to dialyze three times per week. Some VA staff nephrologists may not object to this arrangement with the caveat that Veterans are clearly informed that their choice is not currently the standard of care (17). Patients may elect less frequent dialysis because of reluctance to travel inconvenient distances; skepticism about their need for more frequent hemodialysis therapy or any dialysis at all; involvement with ill family members and children requiring time and attention; or adverse symptoms related to hemodialysis therapy such as post-dialysis fatigue (17). Some patients are extremely debilitated, and have other life-limiting chronic conditions such as malignancy or end-stage liver disease, who stand to gain little in terms of life expectancy and quality of life from more frequent hemodialysis; patients are also sometimes concerned about the impact of dialysis on family members. Hence, we suspect that many Veterans may benefit from having the option of twice-weekly hemodialysis both upon initiation but also during the course of their treatment on dialysis.

**Conclusions and Future Steps**

The overarching objective of implementing incremental and twice-weekly dialysis approaches in the VA dialysis system is to ensure that US Veterans with advanced CKD are given the opportunity for expanded choices of renal replacement therapy. Having this option may be especially valuable in the first 12 months of their transition to ESRD when mortality is the highest (Fig. 1), but may also have relevance at other times (Fig. 5). The incremental dialysis approach can leverage the existing resources of the VA system under experienced clinicians, researchers, and dialysis staff across over 71 VA medical center affiliated dialysis clinics.
nationwide. Thus, based on the emerging evidence this innovative and pragmatic dialysis treatment approach may not only be safe and effective but may improve outcomes of veterans with ESRD, a vulnerable and under-studied population, while helping to overcome existing VA dialysis resource constraints. By implementing incremental dialysis, more Veterans with incident ESRD could be cared for in VA dialysis units (Fig. 4), while also potentially improving patients’ outcomes and containing excess purchased care costs.

There are other important indications for incremental hemodialysis including gradually breaking in new vascular accesses (e.g., arteriovenous fistulas or grafts) to prolong their longevity, and to allow Veterans and their families to better adapt physically, mentally, and emotionally to a dialysis-dependent lifestyle. It also provides a potential middle-ground in the ongoing debate of early versus later initiation of maintenance dialysis, since it offers a more flexible alternative to the abrupt transition to conventional thrice-weekly treatments in lieu of the traditional all-or-none approach of dialysis therapy (17). It may also allow for more gradual escalation from a low protein to high protein diet (for pre-dialysis chronic kidney disease and ESRD patients, respectively). Notably, according to an Italian dialysis experience report, patients who started dialysis therapy on a once-weekly hemodialysis schedule continued a low-protein diet on non-dialysis days, while on dialysis days a high protein diet was provided (31).

We understand that the incremental dialysis approach challenges the current standard of care of conventional thrice-weekly hemodialysis. Indeed, it is less likely that the incremental dialysis approach will be supported by non-governmental dialysis organizations, given perceived reduction in dialysis treatment revenue if twice-weekly hemodialysis is to be implemented among most incident dialysis patients. However, the innovative concept of incremental hemodialysis may support a more patient-centered approach to dialysis prescription. We envision that a randomized-controlled trial of incremental versus conventional thrice-weekly dialysis in VA dialysis centers will examine its safety and efficacy including the preservation of residual kidney function and improvement in patient-centered outcomes and functional status such as health-related quality of life and relevant symptoms related to dialysis treatment (32). The ultimate long-term objective is to provide personalized dialysis therapy that is tailored to patients’ goals, preferences and unique situation in order to optimize survival, health-related quality of life, and other outcomes of importance to patients and their families. The efficient use of resources within the VA dialysis units is well-suited for timely implementation of a large, multi-center controlled trial to address this urgent unmet need in tens of thousands of Veterans nationwide, and the results could potentially impact millions of people with advanced CKD globally.

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