

Does Everyone needs to be on Thrice Weekly Hemodialysis or Less? *Incremental and Twice-weekly HD*

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Journal of Renal Nutrition



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Disclosure of Financial Relationships

Kamyar Kalantar-Zadeh, MD, MPH, PhD

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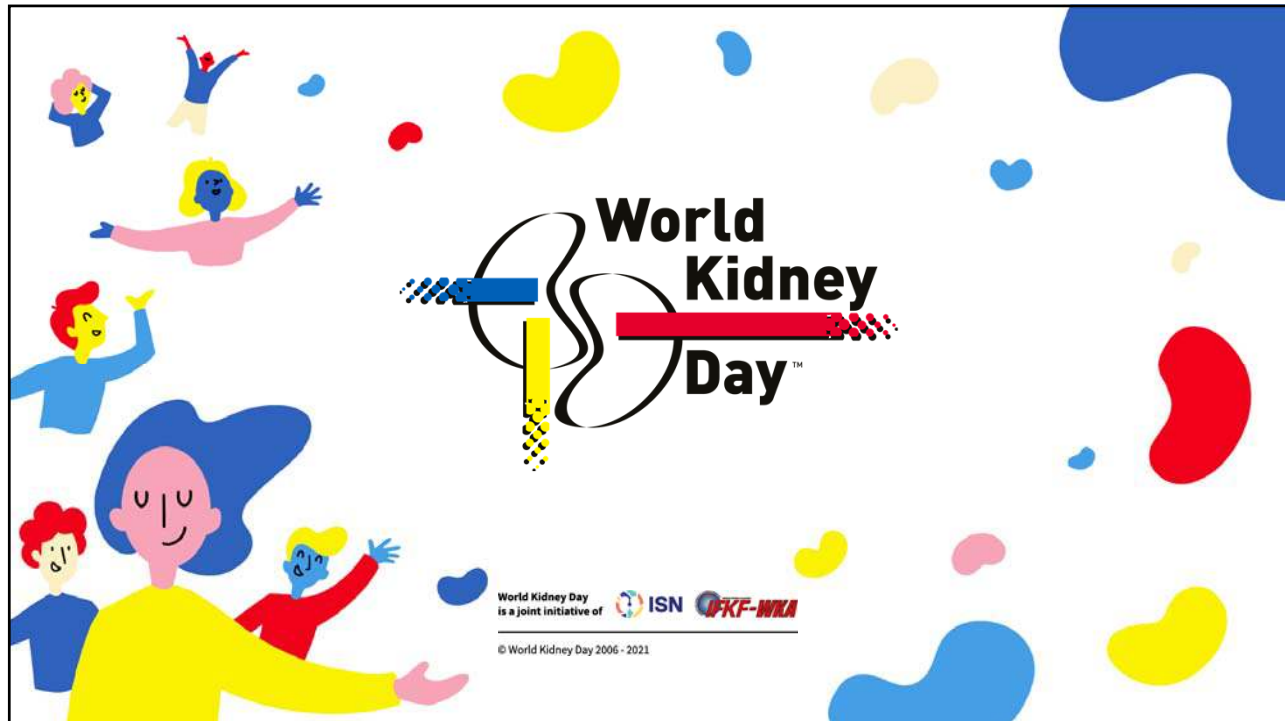
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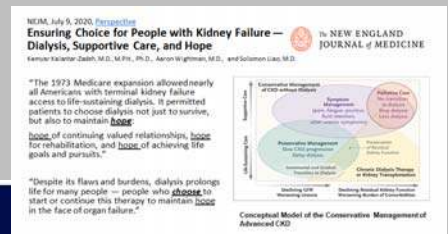
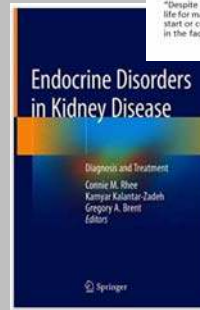
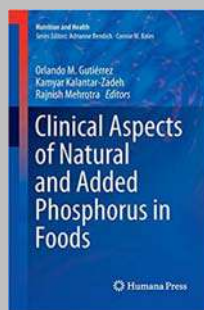
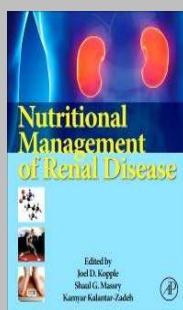
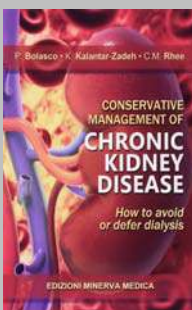
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Sources of this Presentation

4 Textbooks and 2 NEJM Articles:



- Kopple, Massry & Kalantar-Zadeh, Nutritional Management of Renal Disease. 3rd Edition, 2013
- Rhee, Kalantar-Zadeh, Brent, Endocrine Disorders in Kidney Disease, 2019
- Kalantar-Zadeh & Foque, Nutritional Management of CKD. NEJM, 2017
- Kalantar-Zadeh, Wightman and Lia. Ensuring Choice for CKD, Dialysis, Supportive Care and Hope. NEJM, 2020

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Objectives:

1. Review the importance of transition from advanced CKD to ESRD and unanswered questions about dialysis modality.
2. Describe importance of residual kidney function (RKF) upon transition to dialysis.
3. Review the data on incremental transition to dialysis and twice-weekly dialysis start.

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Transition of Care in CKD: BACKGROUND & HYPOTHESES:

- In patients with very late stage (ADVANCED) non-dialysis dependent (NDD) CKD (**eGFR <25** ml/min /1.73 m²) the optimal **transition** of care to **renal replacement therapy (RRT, i.e., dialysis or transplantation)** is not known.

RRT: kidney replacement therapy

Kalantar-Zadeh et al. NDT 2017 [Blueprint of TC-CKD]

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transition

- [tran-zish-uh n, -sish-]
- noun 1. *movement, passage, or change from one position, state, stage, subject, concept, etc., to another;*
- “the transition from adolescence to adulthood.”

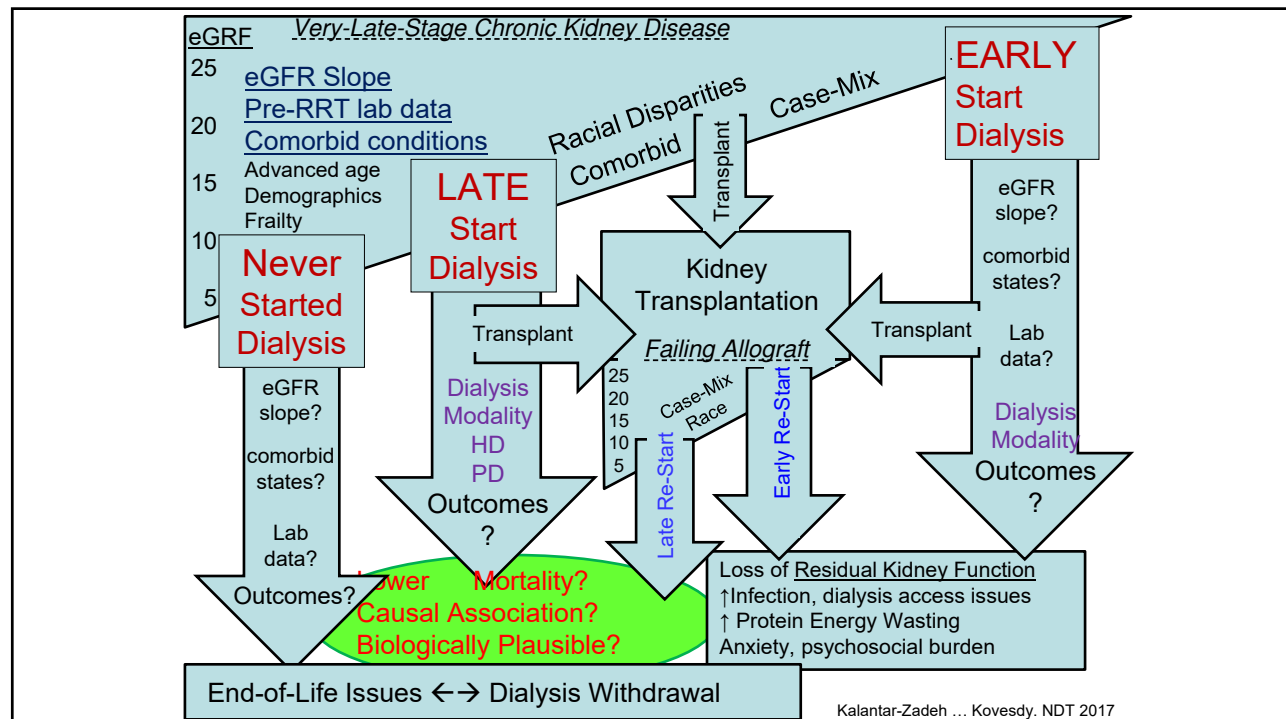
– Dictionary.com

Kalantar-Zadeh et al. NDT 2017 [Blueprint of TC-CKD]

start

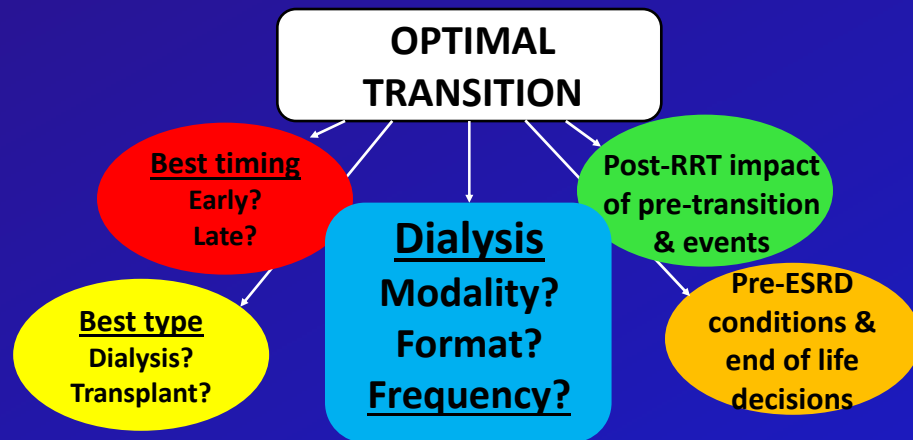
- [stɑːrt]
- 1. to begin or set out, as on a journey or activity.
- 2. to appear or come suddenly into action, life, view, etc.; rise or issue suddenly forth.
- 3. to spring, move, or dart suddenly from a position or place: The rabbit started from the bush.
- 4. to be among the entrants in a race or the initial participants in a game or contest.
- 5. to give a sudden, involuntary jerk, jump, or twitch, as from a shock of surprise, alarm, or pain: The sudden clap of thunder caused everyone to start.

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Questions regarding transition : *Impact of pre-transition conditions?*



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Challenges of Transition Period from NDD to ESRD

1. Higher mortality
2. Higher costs
3. Best timing?
4. Transition of elderly to ESRD
5. Transition across race/ethnicity
6. Residual kidney function
7. Best format? Incremental vs. abrupt

Kalantar-Zadeh et al. *NDT* 2017 [Blueprint of TC-CKD]

Kalantar-Zadeh ... Kovesdy. *NDT* 2017

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Kalantar-Zadeh ... Kovesdy. NDT 2017

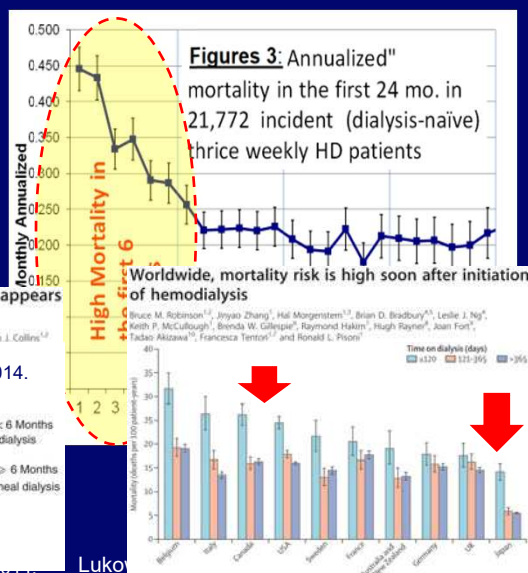
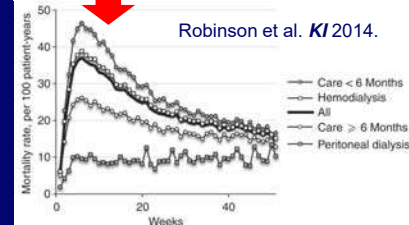
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Challenges of Transition to Dialysis: Very High Early Mortality after Transition

The first 3-6 months of dialysis is associated with an even higher risk of death compared to prevalent dialysis patients.

Early mortality in patients starting dialysis appears to go unregistered

Robert N. Foley^{1,2}, Jinyao Chen¹, Craig A. Sola¹, David T. Gilbertson¹ and Allan J. Collins^{1,2}



Luko

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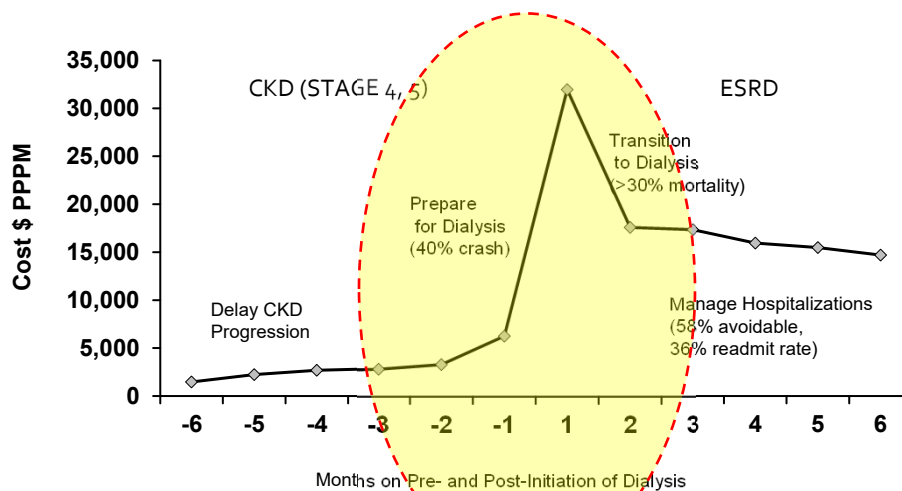
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Costs of CKD to ESRD Transition

AVERAGE \$PPPM COST THROUGH TRANSITION TO DIALYSIS



For Commercial member; based on MarketScan data, from 2010 USRDS ADR, Volume 1, Page 137.
MarketScan is a commercial claims dataset comprised of 10.5 million covered lives that USRDS uses as a benchmark for CKD utilization.

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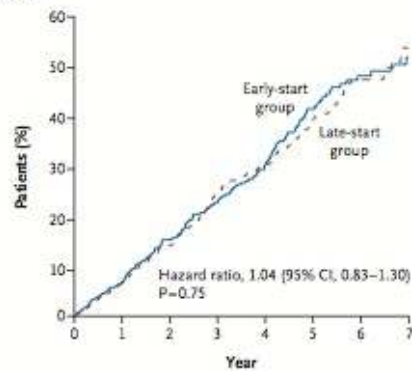
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A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis

Bruce A. Cooper, M.B., B.S., Ph.D., Pauline Branley, B.Med., Ph.D., Liliana Bulfone, B.Pharm., M.B.A., John F. Collins, M.B., Ch.B., Jonathan C. Craig, M.B., Ch.B., Ph.D., Margaret B. Fraenkel, B.M., B.S., Ph.D., Anthony Harris, M.A., M.Sc., David W. Johnson, M.B., B.S., Ph.D., Joan Kesselhut, Jing Jing Li, B.Pharm., B.Com., Grant Luxton, M.B., B.S., Andrew Pilmore, B.Sc., David J. Tiller, M.B., B.S., David C. Harris, M.B., B.S., M.D., and Carol A. Pollock, M.B., B.S., Ph.D., for the IDEAL Study*

N Engl J Med 2010;363:609-19.



No. at Risk								
Early start	404	358	305	249	177	99	59	32
Late start	424	385	333	254	187	115	60	32

Similar survival in early-start and late-start group

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Kalantar-Zadeh et al. NDT 2017 [Blueprint of TC-CKD]

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Transition of Care in ELDERLY and Multi-Morbid CKD Patients

It is not clear whether the poor outcomes of RRT justify these expensive therapies in the elderly esp. if mortality remains essentially unchanged

CONSERVATIVE MANAGEMENT of CKD
Dialysis Free

RRT: kidney replacement therapy

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Kalantar-Zadeh et al. NDT 2017 [Blueprint of
TC-CKD]

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Blacks are more likely to be a dialysis patient:
US General Population: 14% Blacks
US Dialysis Population: 35% Blacks

*Black Americans have lower
life expectancy than white*

African American paradox

*White Americans have lower life
expectancy than Blacks.*



Kalantar-Zadeh et al, Seminars in Dialysis 2010

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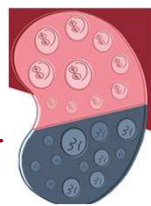
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Residual Kidney Function (RKF) upon Transition and Dialysis Patients

Therapeutic options

- Avoidance of nephrotoxins
- RAAS blockade
- BP control?
- Avoidance of hypovolemia
- ↓ Peritonitis in PD
- START Twice-Weekly HD**
- Low protein diet ?



Benefits of RKF

- ↑ middle molecule & uremic toxins
- Maintenance of liquid balance
- Improved BP control & ↓ in LVH
- Endocrine: Epo, Ca⁺⁺, Pi, VitD3
- ↓ Malnutrition and inflammation
- ↓
- ↑ Survival & quality of life

Am J Kidney Dis 53:1068-1081. © 2009

Kalantar-Zadeh et al 2019 for 2017 [Blueprint of TC-CKD]

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Residual Kidney Function (RKF)

RKF declines more rapidly in patients on HD than PD therapy.

- Shafi et al, CHOICE Study (AJKD 2010):
617 of 734 (**84%**) HD patients reported good urine output at baseline, **but only 28% had acceptable RKF after 1 year.**
- Preserved RKF was associated with **lower mortality** (hazard ratio, **0.70**, 95% CI: 0.52-0.93) and **better HRQoL**, lower CRP ($P = 0.02$) and interleukin 6 ($P = 0.03$) levels, and 12,000-U/wk lower erythropoietin doses ($P < 0.001$).¹⁵

Shafi, T., Jaar, B.G., Plantinga, L.C. et al. Association of residual urine output with mortality, quality of life, and inflammation in incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study. *Am J Kidney Dis.* 2010; 56: 348–358

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Kalantar-Zadeh et al. NDT 2017 [Blueprint of TC-CKD]

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Dialysis Treatment Frequency

Discussion: Twice vs. Thrice Weekly

FROM THE EDITOR

How About Twice-Weekly Hemodialysis?

In recent trips to India, China, Brazil, and other countries, I was intrigued by large numbers of patients with end-stage renal disease who underwent hemodialysis (HD) less frequently than three times a week. Indeed, I encountered sporadic patients who received HD as infrequently as only once to twice a month! Dialysis treatment time could be as short as two to three hours per session. I was told that these patients



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May 2012

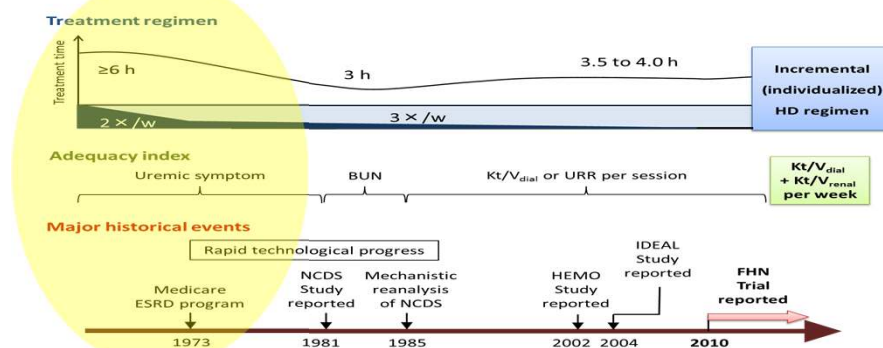
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Historical Change in Hemodialysis Regimen

(Adapted from Lacson E, Jr. and Brunelli SM. Clin J Am Soc Nephrol 2011;6:2522-30.)



Frequency and duration of HD were empirically determined following Scribner's invention of a

Malignant hypertension due to hypervolemia and uremia-associated peripheral neuropathy necessitated an intensification of treatment to twice-weekly therapy.

The 12 to 20 hour twice-weekly schedule was too burdensome on patients and families, and a 6

When the Medicare ESRD Program came into being in 1973, thrice-weekly dialysis was the usual practice and provided a concession between delivery of adequate therapy and treatment of the most patients using limited resources.

Obi Y, Eriguchi R, Ou SM, Rhee CM, Kalantar-Zadeh K.
Blood Purification. 2015 Nov;40(4):298-305.

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Incremental HD and Residual Kidney Function (RKF)

- Incremental dialysis has been used successfully in the initiation of **PERITONEAL Dialysis** therapy.
- Termorshuizen et al,¹⁹ Bargman et al,²⁰ and Szeto et al,²¹
 - in patients with substantial RKF, dialysis dose did not have a significant impact on outcomes.
- *Therefore we must revisit the topic of incremental HD and plan **randomized controlled trials** to explore the hypothesis that transitioning to ESRD with incremental HD may*
 - preserve RKF longer, and
 - decrease mortality during the first year of HD therapy.

Adapted from:
Rhee et al. *Seminars in Dialysis* 2014
Kalantar-Zadeh et al *Am J Kidney Dis* 2014
Kalantar-Zadeh & Casino. *Nephrol Dial Transplant* 2014

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Less Frequent (Incremental) Hemodialysis Transition

- **Originally described for PD patients**
 1. Main Goal: To preserving **Residual Kidney Function (RKF)**
RKF plays an important role for solute removal, fluid balance, survival
 - Additional Goals:
 1. **Smoother** (gradual) transition vs. abrupt start
 2. More patient **freedom** and greater **quality of life** (?)
 3. Protecting **AV Fistula** longer,
 4. Less dialytic **nutrient loss, less inflammation, less infection, less blood loss**
 5. **Cost-saving** for the payer (3 pts on 2x/week instead of 2 pts on 3x/week)
(but less beneficial and more challenging for the provider?)
- **Potential indications for infrequent (incremental) HD**
 - 1) Gradual transition to HD/PD with good RKF (see criteria, next)
 - 2) Return to dialysis Rx upon gradual allograft failure
 - 3) Conversion from failing PD to HD
- **Potential Approaches**
 - Dose of delivered dialysis increased as RKF declines
→ sum of weekly RKF plus dialytic clearance is maintained
 - Concurrent dietary protein restriction (?)

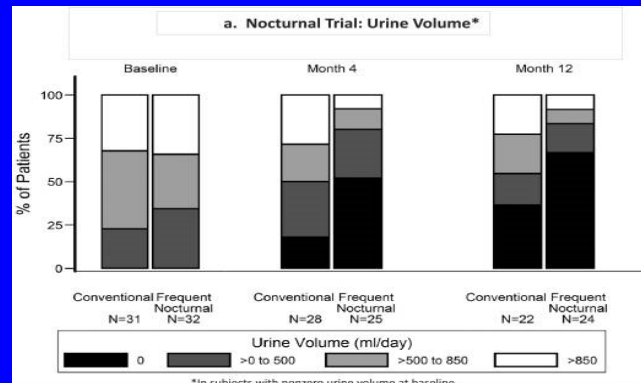
Adapted from:
Rhee et al. *Seminars in Dialysis* 2014
Kalantar-Zadeh et al *Am J Kidney Dis* 2014
Kalantar-Zadeh & Casino. *Nephrol Dial Transplant* 2014

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USA Frequent Hemodialysis Network (FHN): Frequent Nocturnal HD Accelerated the LOSS of Residual Kidney Function!

- In the **frequent** dialysis group, urine volume had **declined** to zero in 52% and 67% of patients at months 4 and 12, respectively, compared with 18% and 36% in controls.

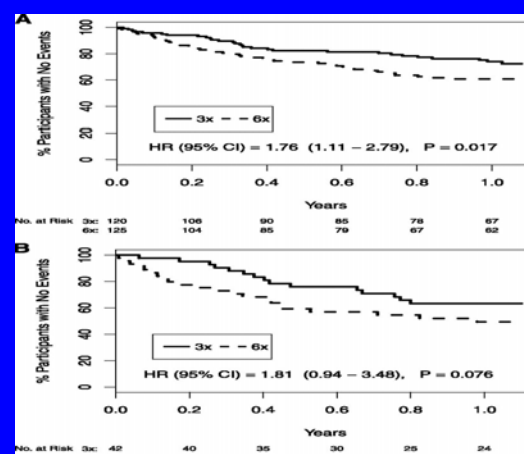


Daugirdas JT1, Greene T, Rocco MV, Kaysen GA, Depner TA, Levin NW, Chertow GM, Ornt DB, Raimann JG, Larive B, Kliger AS; FHN Trial Group.. Effect of frequent hemodialysis on residual kidney function. *Kidney Int.* 2013; 83: 949–958

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USA Frequent Hemodialysis Network (FHN): Frequent hemodialysis increases the risk of vascular access complications

- Frequent hemodialysis increases the risk of vascular access complications.
- The nature of the **AV access repairs** suggests that **this risk likely results from increased hemodialysis frequency** rather than heightened surveillance.
- Kaplan-Meier curves of time to first access repair, access loss, or access hospitalization.



Rita S. Suri et al. *JASN* 2013;24:498-505

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Twice-Weekly and Incremental Hemodialysis Treatment for Initiation of Kidney Replacement Therapy

Kamyar Kalantar-Zadeh, MD, MPH, PhD,^{1,2} Mark Unruh, MD,³ Philip G. Zager, MD,³
Csaba P. Kovesdy, MD,⁴ Joanne M. Bargman, MD,⁵ Jing Chen, MD,⁶
Suresh Sankarasubaiyan, MD,⁷ Gaurang Shah, MD,² Thomas Golper, MD,
Richard A. Sherman, MD,⁹ and David S. Goldfarb, MD¹⁰

Kalantar-Zadeh K et al., Am J Kidney Dis. 2014 Aug;64(2):181-6.



Seminars in Dialysis TRANSITION TO DIALYSIS: CONTROVERSIES IN ITS TIMING AND MODALITY

Infrequent Dialysis: A New Paradigm for Hemodialysis Initiation

Connie M. Rhee,* Mark Unruh,† Jing Chen,‡ Csaba P. Kovesdy,§¶ Phillip Zager,†**
and Kamyar Kalantar-Zadeh*

Rhee CM et al., Semin Dial. 2013 Nov-Dec;26(6):720-7

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Twice-Weekly Dialysis Rx Metrics

1. Good RKF with at least half a liter/d urine output: **UOP >0.5 L/day (>600 cc/day)**
2. **Urea Clearance (KRU) > 3 ml/min (transition to 3x/wk of KRU <2 ml/min)**
3. Limited fluid retention : IDWG <2.5 kg (or <5% of ideal dry weight) without HD for 3-4 d
4. Limited or manageable CV or pulmonary Sx without clinically significant fluid overload
5. Suitable body size relative to RKF (larger pts OK for 2x/wk HD if not hypercatabolic)
6. Hyperkalemia (K > 5.5 mEq/L) is infrequent or readily manageable
7. Hyperphosphatemia (P > 5.5 mg/dL) is infrequent or readily manageable
8. Good nutritional status without florid hypercatabolic state
9. Lack of profound anemia (Hb >8 g/dL) and appropriate responsiveness to anemia therapy
10. Infrequent hospitalization and easily manageable comorbid conditions
11. Satisfactory health-related quality of life

Implementation Strategies

- A. To initiate and maintain 2x/wk HD, the pt should meet **first criterion (UOP >0.5 L/d)** plus most (5 out of 9) other criteria
- B. Examine these criteria every month and compare outcome between 2x/wk and 3x/wk HD to ensure outcome non-inferiority for continuation of 2x/wk HD
- C. Consider transition to 3x/wk HD regimen if patient's UOP decreases (<0.5 L/d) or patient's nutritional status or general health condition shows a deteriorating trend over time

Kalantar-Zadeh ... Goldfarb, AJKD 2014



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What does KDOQI say?

- ... the Work Group decided that thrice-weekly HD as a minimum frequency level was no longer appropriate.
- Based on solute kinetics, the Work Group was comfortable recommending a twice-weekly dialysis schedule but **only for patients with substantial RKF ($KRU \geq 3$ mL/min per 1.73 m²)**
- If Total standard Kt/V = 2.0 per week

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AJKD
Perspective

Twice-Weekly and Incremental Hemodialysis Treatment for Initiation of Kidney Replacement Therapy

Kamyar Kalantar-Zadeh, MD, MPH, PhD,^{1,2} Mark Unruh, MD,³ Phillip P. Tsai,⁴ Csaba P. Kovesdy, MD,⁴ Joanne M. Bargman, MD,⁵ Suresh Sankarasubbaiyan, MD,⁷ Gaurang Shah,⁸ Richard A. Sherman, MD,⁹ and ...

Nephrol Dial Transplant (2014) 29: 1618–1620
doi: 10.1093/ndt/gfu096
Advance Access publication 29 April 2014

American Journal of Kidney Disease 2014

Association of Initial Twice-Weekly Hemodialysis Treatment with Preservation of Residual Kidney Function in ESRD Patients

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Seminars in Dialysis

TRANSITION TO DIALYSIS: CONTROVERSIES IN ITS TIMING AND MODALITY

Seminars in Dialysis 2014

Infrequent Dialysis: A New Paradigm for Hemodialysis Initiation

Connie M. Rhee,* Mark Unruh,† Jing Chen,‡ Csaba P. Kovesdy,§¶ Phillip Zager,†** and Kamyar Kalantar-Zadeh*

Reactions to 2x/week papers in Nephrology journals

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Twice-Weekly HD and RKF: Shanghai Data

Nephrology
American Journal of

Original Report: Patient-Oriented, Translational Research

Am J Nephrol 2014;40:140–150
DOI: 10.1159/000365819

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Association of Initial Twice-Weekly Hemodialysis Treatment with Preservation of Residual Kidney Function in ESRD Patients

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- Residual kidney function (RKF) has consistently been a predictor of greater survival in maintenance hemodialysis (HD) patients.
- The relationship between HD treatment frequency and RKF preservation has not been well examined.
- We hypothesized that initial twice-weekly HD helps maintain a longer RKF.

Minmin Zhang, Mengjing Wang, Haiming Li ... Jing Chen..., *Am J Nephrol* 2014

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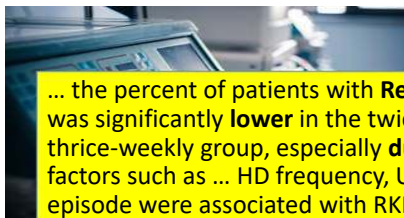
• Study Shows Benefit of Twice-Weekly Hemodialysis

September 02, 2014
[General News](#)

Renal & Urology News

Study Shows Benefit of Twice-Weekly Hemodialysis

Better preservation of residual kidney function with twice-weekly in first year. Twice-weekly hemodialysis (HD) during the first year of dialysis treatment is associated with better preservation of residual kidney function (RKF) compared with thrice-weekly HD, according to a new study.



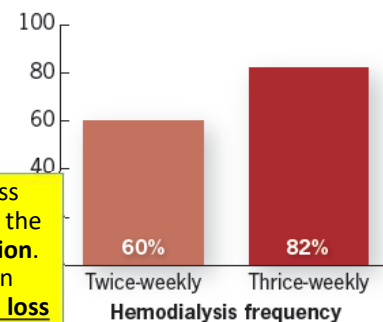
... the percent of patients with **Residual Kidney Function (RKF)** loss was significantly **lower** in the twice-weekly group compared with the thrice-weekly group, especially **during the first year of HD initiation**. factors such as ... HD frequency, URR and intradialytic hypotension episode were associated with RKF loss, and the **odds ratio of RKF loss for each additional HD treatment per week was 7.2.**

Conclusion: Twice-weekly HD during the first year of dialysis therapy appears to be associated with better RKF preservation

Jody Charnow

Twice-Weekly vs. Thrice Weekly HD

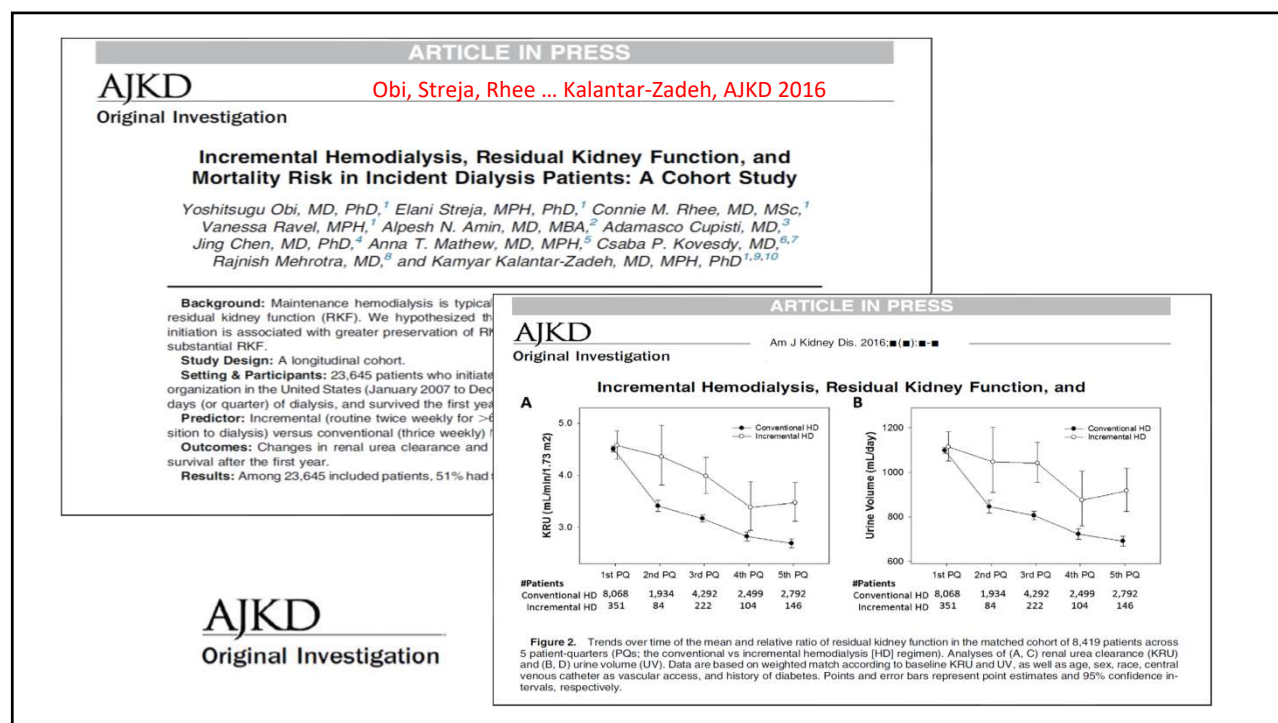
In a study, the proportion of patients who lost residual kidney function was lower with twice-weekly than thrice-weekly hemodialysis.



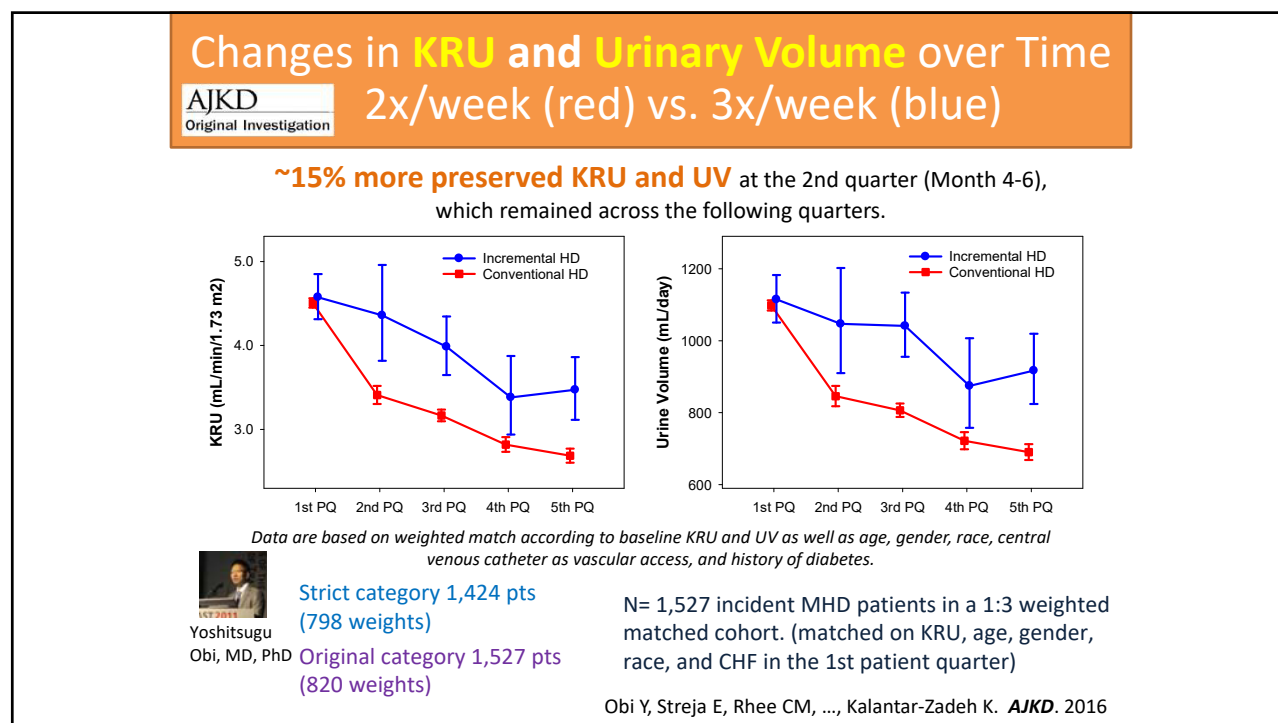
Chen J, et al. Association of initial twice-weekly dialysis treatment with preservation of residual kidney in ESRD patients. *Am J Nephrol* 2014;40:140-150.

Minmin Zhang, Mengjing Wang, Haiming Li ... Jing Chen..., *Am J Nephrol* 2014

38

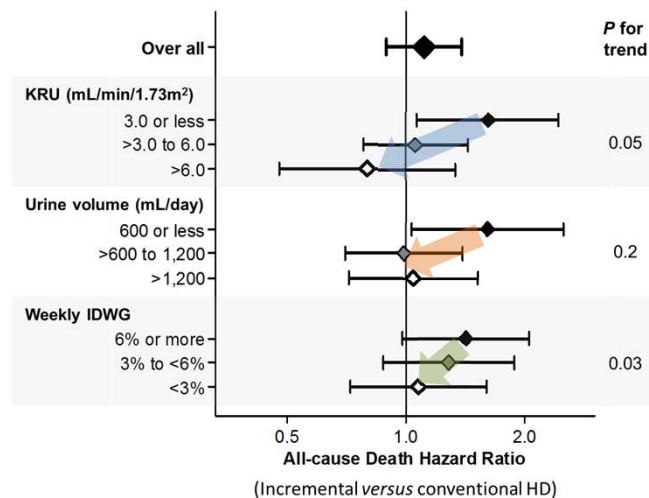


39



40

The mortality risk of incremental HD appeared to be *dependent on patients' residual kidney function.*



Obi Y, Streja E, Rhee CM, ..., Kalantar-Zadeh K.
AJKD. 2016 .

41

Obi, Rhee, Matthew ... Kalantar-Zadeh, JASN 2016

CLINICAL EPIDEMIOLOGY www.jasn.org

JASN

Residual Kidney Function Decline and Mortality in Incident Hemodialysis Patients

Yoshitsugu Obi,* Connie M. Rhee,* Anna T. Mathew,[†] Gaurang Shah,* Elani Streja,* Steven M. Brunelli,[‡] Csaba P. Kovesdy,^{§||} Rajnish Mehrotra,[¶] and Kamyar Kalantar-Zadeh* **††

*Harold Simmons Center for Kidney Disease Research and Epidemiology, Division of Nephrology and Hypertension,

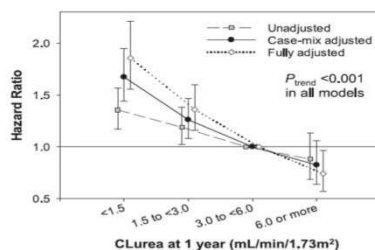
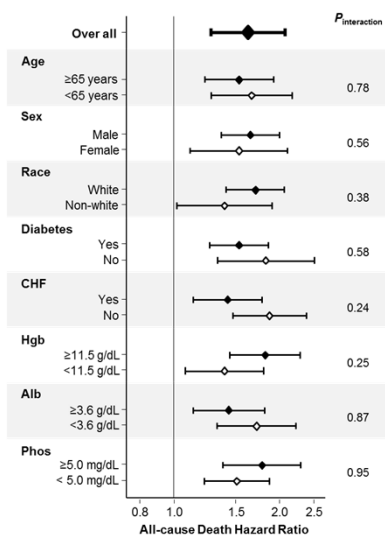


Figure 1. Renal CL_{urea} and all-cause mortality risk in incident hemodialysis patients. The mortality risk associated with renal CL_{urea} at 1 year after initiating dialysis among 6538 incident hemodialysis patients (2007–2010) with three levels of adjustment.

42

Figure 4. Over all and subgroup analyses of association between **rapid decline** in $CL_{urea} > 3 \text{ mL/min/1.73m}^2/\text{year}$ and all-cause **mortality** among 6,538 incident HD patients (2007-2010) in the case-mix adjustment model.



*Robust against
subgroup analyses*

JASN

Obi Y, Rhee CM, Mathew AT, ..., and Kalantar-Zadeh K.
Residual Kidney Function Decline and Mortality in Incident Dialysis Patients.
J Am Soc Nephrol. 2016.

43

Do hemodialysis patients with substantial Residual Kidney Function (RKF) exhibit the expected better survival at higher hemodialysis doses?

Nephrol Dial Transplant (2018) 1-9
doi: 10.1093/ndt/gfy060

ndt
Nephrology Dialysis Transplantation

Impact of residual kidney function on hemodialysis adequacy and patient survival

Mengjing Wang^{1,2*}, Yoshitsugu Obi^{1*}, Elani Streja^{1,3}, Connie M. Rhee^{1,3}, Jing Chen², Chuanming Hao², Csaba P. Kovacs^{4,5} and Kamyar Kalantar-Zadeh^{1,3,6}

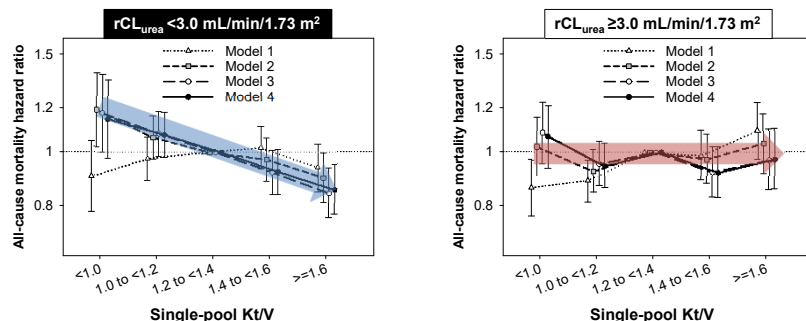
¹Harold Simmons Center for Kidney Disease Research and Epidemiology, Division of Nephrology and Hypertension, Department of Medicine,

2021/2/13

44

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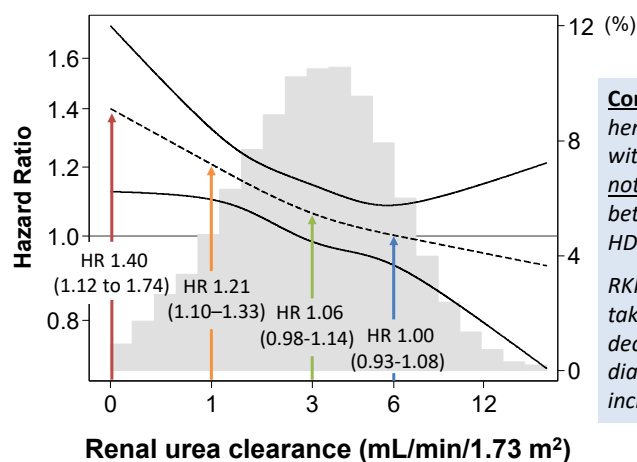
In the primary adjustment model (Model 3),
there was a significant trend toward
higher mortality across lower spKt/V categories
among patients with low rCL_{urea}
but NOT among those with high rCL_{urea}
($P_{\text{trend}} < 0.001$ and 0.4, respectively).



Wang MJ, Obi Y, Streja E, Rhee CM, ..., and Kalantar-Zadeh K.
Nephrol Dial Transplant. 2018 in press.

45

The risk associated with low spKt/V (i.e., <1.2 vs. ≥1.2)
was **linearly attenuated with greater rCL_{urea}**.



Conclusions: Incident hemodialysis patients with substantial RKF do not exhibit the expected better survival at higher HD doses.

RKF levels should be taken into account when deciding on the dose of dialysis treatment among incident HD patients.

Wang MJ, Obi Y, Streja E, Rhee CM, ..., and Kalantar-Zadeh K.
Nephrol Dial Transplant. 2018 in press.

46

Treatment frequency and mortality among incident hemodialysis patients in the United States comparing incremental with standard and more frequent dialysis

Anna Mathew, MD, MPH^{1,9}, Yoshitsugu Obi, MD, PhD^{2,9}, Connie M. Rhee, MD, MSc², Joline L.T. Chen, MD, MS³, Gaurang Shah, MD², Wei-Ling Lay, MD², Csaba P. Kovacs, MD^{4,5}, Rajnish Mehrotra, MD, MS⁶ and Kamyar Kalantar-Zadeh, MD, MPH, PhD^{2,7,8}

¹Division of Nephrology, Northwell Health, Great Neck, New York, USA; ²Harold Simmons Center for Kidney Disease Research and Epidemiology, Division of Nephrology and Hypertension, University of California Irvine, School of Medicine, Orange, California, USA; ³Division of Nephrology, VA Long Beach Healthcare System, Long Beach, California, USA; ⁴Division of Nephrology, University of Tennessee

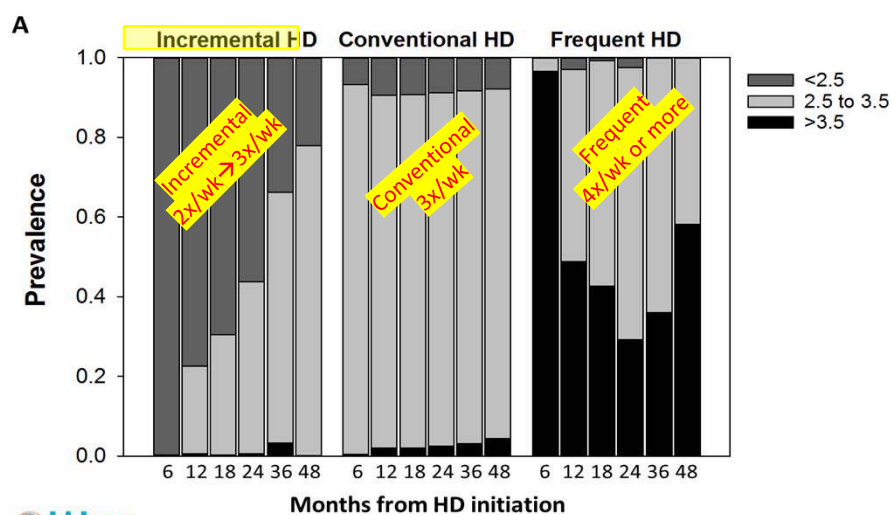
Treatment frequency and mortality among incident hemodialysis patients in the United States comparing incremental with standard and more frequent dialysis

2021/2/13

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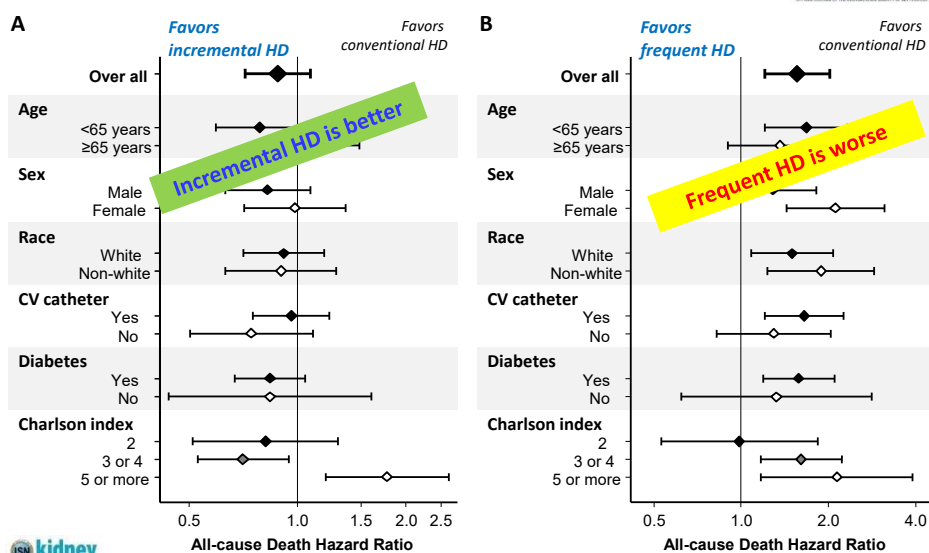
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Figure 1. The distribution of quarterly-averaged (A) treatment frequency per week and (B) treatment time in minutes per session across the hemodialysis (HD) regimen groups in the matched cohort of 50,756 incident hemodialysis patients.



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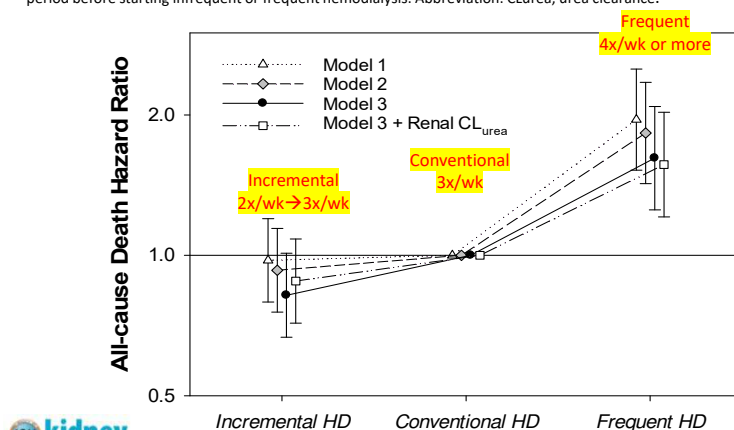
Figure 4. Overall and subgroup analyses of the association between hemodialysis (HD) regimen and all-cause mortality risk; (A) incremental HD vs. conventional HD and (B) frequent HD vs. conventional HD. Data are based on weighted match according to age, sex, race, central venous (CV) catheter as vascular access, and the Charlson comorbidity index. Hazard ratios were from the fully adjusted model including renal urea clearance.



Mathew, Obi Y, Rhee CM, ..., and Kalantar-Zadeh K. Treatment frequency and mortality among incident hemodialysis patients in the United States comparing incremental with standard and more frequent dialysis. *Kidney Int.* 2016

49

Figure 3. Adjusted all-cause mortality risk of incremental and frequent hemodialysis (HD) in the matched cohort (n=50,756). Weighted coarsened exact matching were employed based on age, sex, race, central venous catheter as vascular access, diabetes, and the Charlson comorbidity index. Model 1 is the unadjusted model. Model 2 includes Medicare as primary insurance, spKt/V, body mass index, hemoglobin, albumin, corrected calcium, iron saturation, and bicarbonate, and log-transformed ferritin and intact parathyroid hormone (iPTH). Model 3 includes variables in Model 2, a history of fluid overload, interdialytic weight gain, creatinine, phosphorus. Data on laboratories were extracted during the first 91 days of dialysis and those except for ferritin and iPTH were further restricted to the initial thrice-weekly hemodialysis period before starting infrequent or frequent hemodialysis. Abbreviation: CL_{urea}, urea clearance.



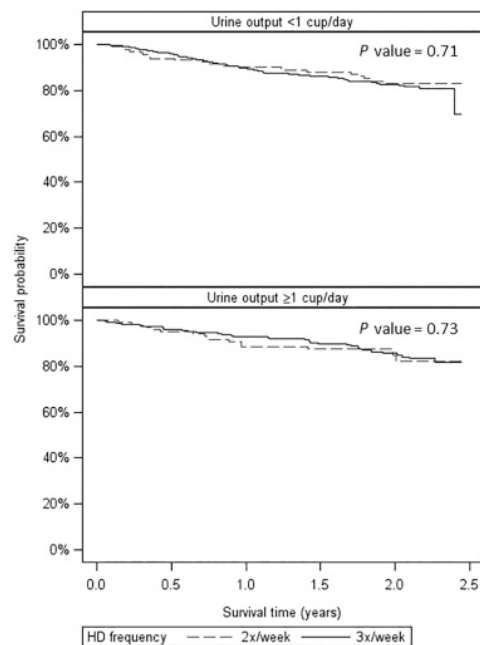
Mathew, Obi Y, Rhee CM, ..., and Kalantar-Zadeh K. Treatment frequency and mortality among incident hemodialysis patients in the United States comparing incremental with standard and more frequent dialysis. *Kidney Int.* 2016 in press.

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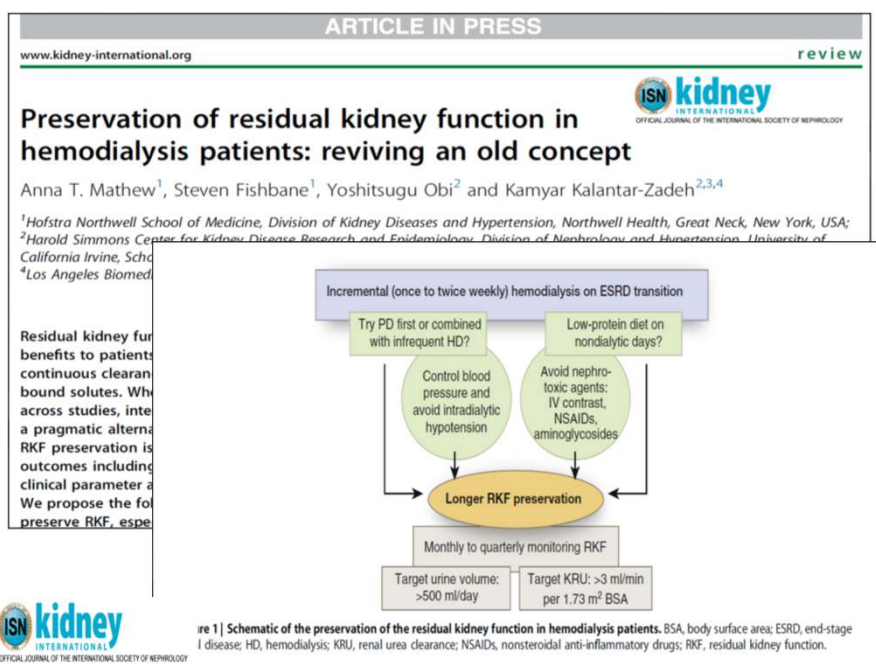
Twice-weekly data from China

Cohort derived from 15 units randomly selected from each of 3 major cities (total N = 45), we generated a [propensity score](#) for the probability of dialysis frequency assignment, estimated a survival function by propensity score quintiles, and averaged stratum-specific survival functions to generate mean survival time. We used the proportional rates model to assess hospitalizations. We stratified all analyses by RKF, as reported by patients (urine output <1 vs. ≥ 1 cup/day).


Yan...Anand
Kidney Int Rep 2018




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말기신부전 임상연구센터
Clinical Research Center for End-stage Renal Disease

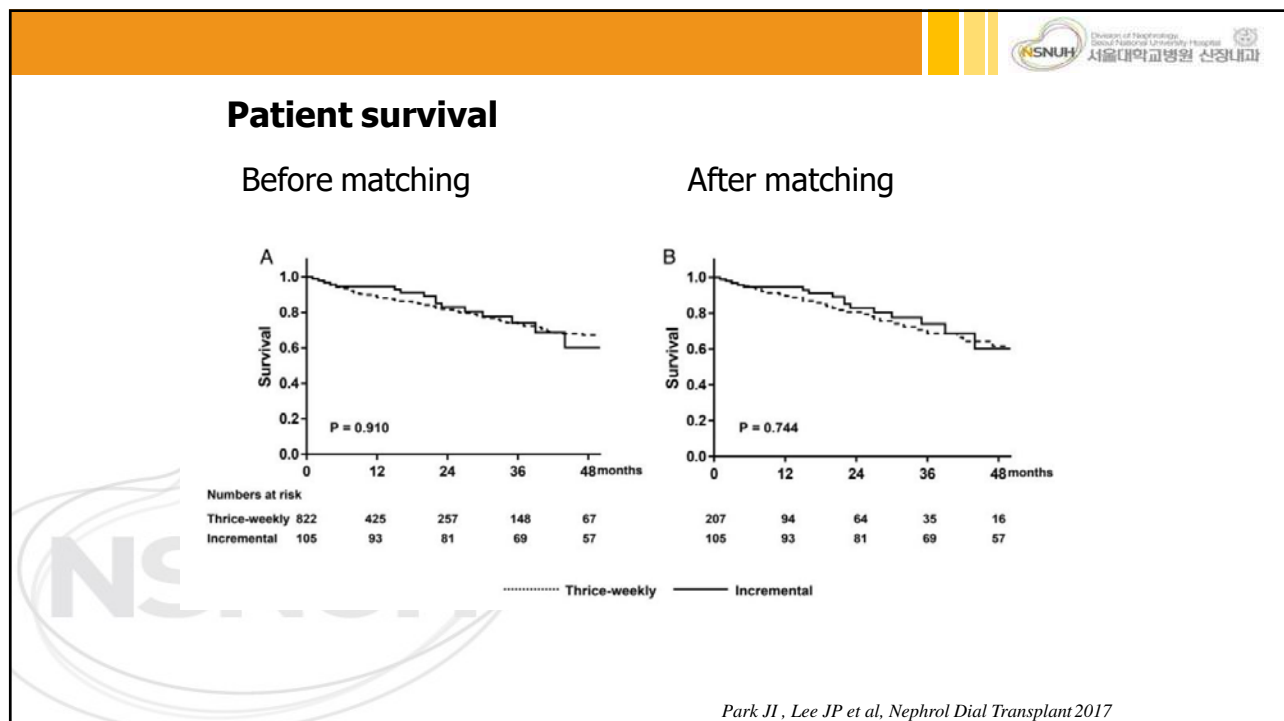
Nephrol Dial Transplant (2017) 32: 355–363
doi: 10.1093/ndt/gfw332
Advance Access publication 28 September 2016

Comparison of outcomes between the incremental and thrice-weekly initiation of hemodialysis: a propensity-matched study of a prospective cohort in Korea

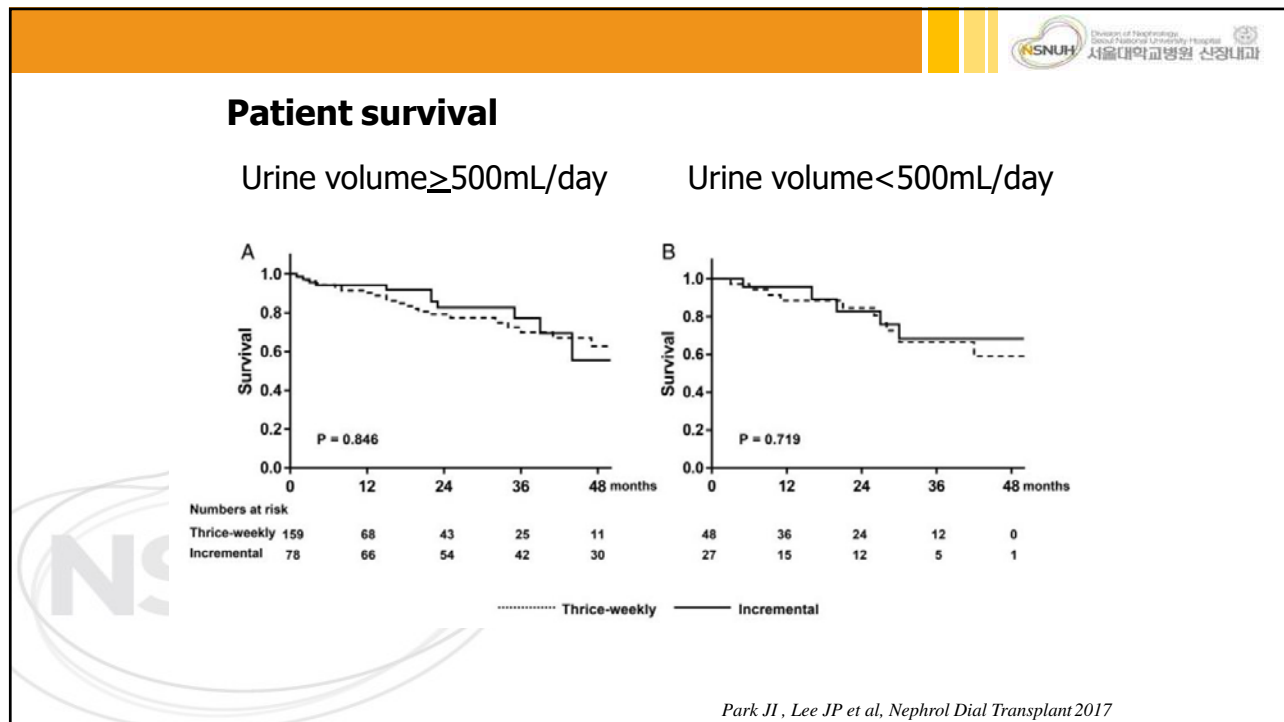
Ji In Park^{1,2}, Jung Tak Park^{2,3}, Yong-Lim Kim^{2,4}, Shin-Wook Kang^{2,3}, Chul Woo Yang^{2,5}, Nam-Ho Kim^{2,6}, Yun Kyu Oh^{2,7}, Chun Soo Lim^{2,7}, Yon Su Kim^{2,8} and Jung Pyo Lee^{2,7} on behalf of the CRC for ESRD
Investigators

Park JI, Lee JP et al, Nephrol Dial Transplant 2017

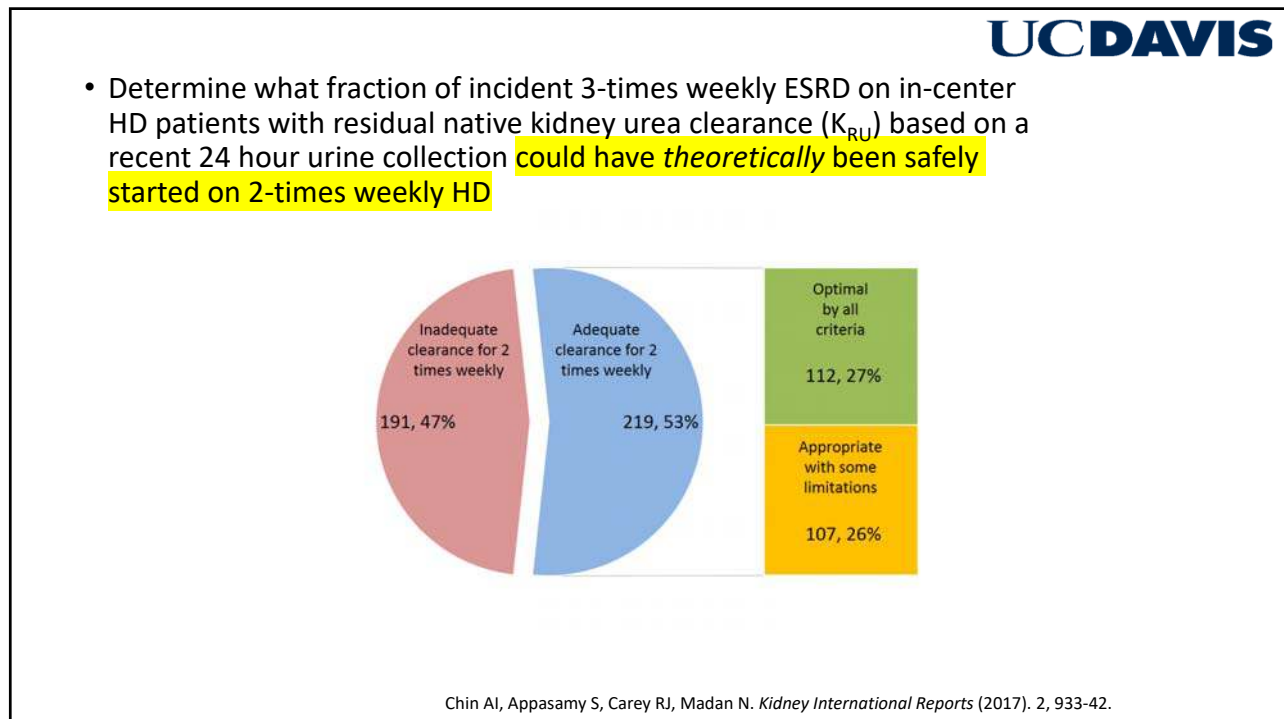
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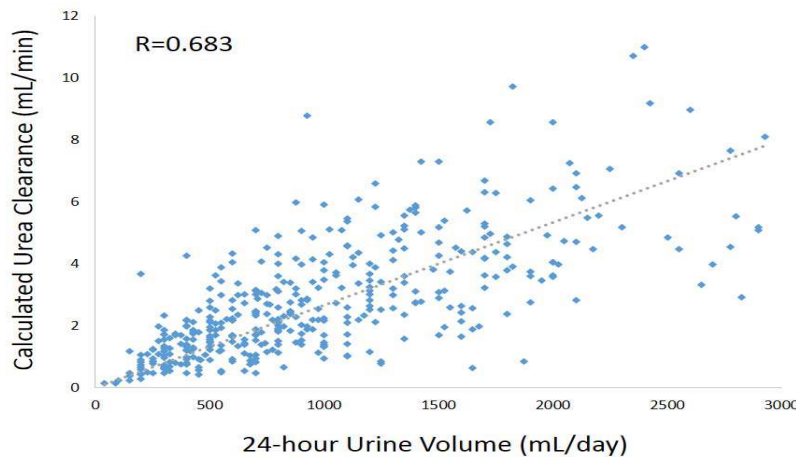


55



56

Urine volume alone is a (poor) estimate of urea clearance?



Chin AI, Appasamy S, Carey RJ, Madan N. *Kidney International Reports* (2017). 2, 933-42.

57

Combined Diet-Dialysis Program.....

- An Integrated and **incremental** strategy
- Gradual transition to hemodialysis while keeping Low Protein Diet

Caria et al. *BMC Nephrology* 2014, 15:172
<http://www.biomedcentral.com/1471-2369/15/172>



RESEARCH ARTICLE

Open Access

The incremental treatment of ESRD: a low-protein diet combined with weekly hemodialysis may be beneficial for selected patients

Stefania Caria^{1*}, Adamasco Cupisti², Giovanna Sau³ and Piergiorgio Bolasco¹

Caria S, Cupisti A, Sau, Bolasco. *BMC Nephrol* 2014;15:172

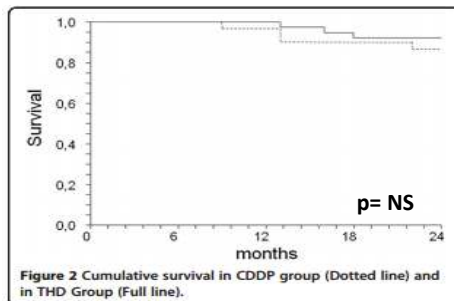
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The incremental treatment of ESRD: a low-protein diet combined with weekly hemodialysis may be beneficial for selected patients

Stefania Caria^{1*}, Adamasco Cupisti², Giovanna Sau³ and Piergiorgio Bolasco¹

- LPD enables to adapt infrequent dialysis
 - 24-months multicenter prospective study with 68 CKD-5 patients.
 - Once weekly dialysis with LPD under dietitian counselling (CDDP) vs. thrice weekly dialysis (THD)



- Survival in 24 months was not different (94.7% vs 86.8% in CDDP vs THD).
- However, **hospitalization, prescribed medications and medical cost** were higher in pts with thrice weekly dialysis.

2016/10/5

Caria S et al. BMC nephrol 2014

59

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Nutritional Management of Incremental HD: strategies for dialysis commencing: **once weekly** → **2x/week** → **3x/week**

	Once-a-week	Twice-a-week	Thrice-a-week
Nutritional support	+++	++	+
Protein intake	Reduced (6 out of 7 days): sVLDP	Reduced (5 days): sVLDP or LPD	increased
Energy intake	increased	increased	increased
vascular access compromise	+	++	+++
Protection of residual renal function	+++	++	-/+
"Counter-Physiologic" effect of HD treatment	+	++	+++
HD scheduling challenge	+	++	-
Costs and reimbursement	+	++	+++

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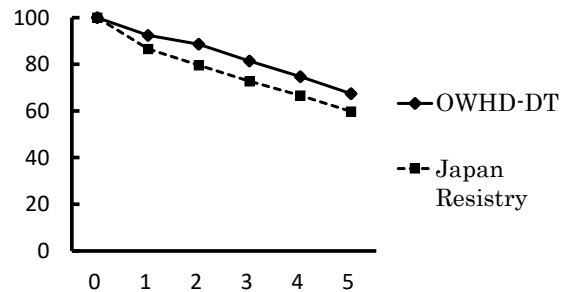
Caria S, Cupisti A, Sau, Bolasco. *BMC Nephrol* 2014;15:172
Bolasco, Cupisti, Locarelli, Caria, Kalantar-Zadeh, *J Ren Nutr*. 2016 26:352-359

60

Japanese Data: Once-weekly hemodialysis combined with low-protein and low-salt dietary treatment as a favorable therapeutic modality for selected patients with end-stage renal failure: a prospective observational study in Japanese patients

**Nakao T, Kanazawa Y,
Takahashi T**

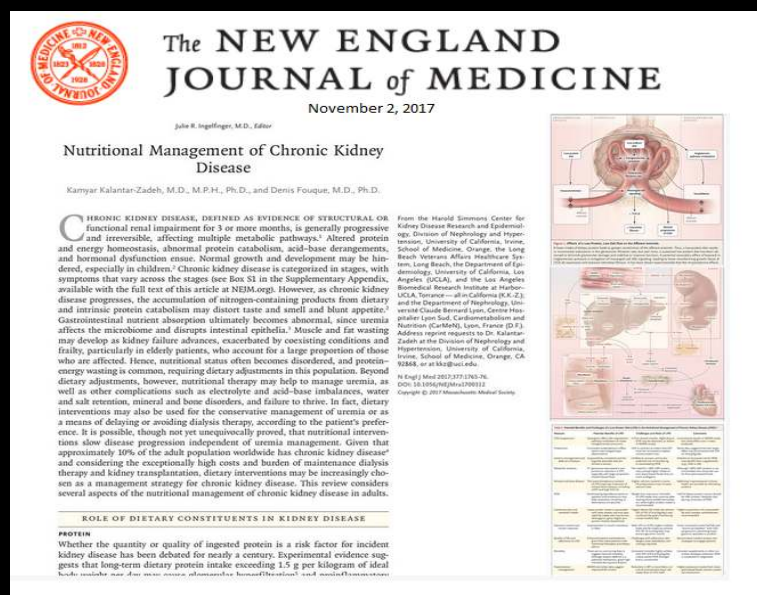
**Organization for Kidney
and Metabolic Disease
Treatment**



BMC Nephrology 2018; 19: 151

Nakao T, et al: BMC Nephrol, 2018; 19:151

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**Kalantar-Zadeh & Fouque, Nutritional Management of CKD.
NEJM Nov 2, 2017**

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Low Protein Diet for CKD-ESRD Transition

Table 2. Recommended Dietary and Nutrient Intake in Adults, According to the CKD Stage.*

Dietary Constituent	Normal Kidney Function with Increased CKD Risk	Mild-to-Moderate CKD†	Advanced CKD‡	Transition to Dialysis§	Ongoing Dialysis or Any Stage with Existing or Imminent PEW
Protein (g/kg/day)	<1.0; increase proportion of plant-based proteins	<1.0 (consider 0.6–0.8 if eGFR <45 ml/min/1.73 m² or rapid progression)	0.6–0.8, including 50% HBV protein, or <0.6 with addition of EAA or KA	0.6–0.8 on nondialysis days and >1.0 on dialysis days	1.2–1.4; may require >1.5 if hypercatabolic state develops
Plant-based foods (g/day)	25–50% higher proportion (>50%) of plant-based foods (e.g., DASH diet)	25–50% higher proportion (>50%) of plant-based foods	25–50% higher proportion (>50%) of plant-based foods	25–50% or more	25–50% or more, suggesting strict vegan diet
Energy (kcal/kg/day)**	30–35; adjust to target weight reduction if BMI >30††	30–35; increase proportion with LPD	30–35; increase proportion with LPD	30–35	30–35; target higher intake if PEW present or imminent
Fats	Mostly monounsaturated and polyunsaturated lipids, including n-3 fatty acids	Mostly monounsaturated and polyunsaturated lipids, including n-3 fatty acids; increase proportion with low-protein intake	Mostly monounsaturated and polyunsaturated lipids, including n-3 fatty acids; increase proportion with low-protein intake	Mostly monounsaturated and polyunsaturated lipids, including n-3 fatty acids	Mostly monounsaturated and polyunsaturated lipids, including n-3 fatty acids

* Normal kidney function is defined as an estimated GFR (eGFR) of at least 60 ml per minute per 1.73 m² of body-surface area. Patients in this category do not have substantial proteinuria but are at increased risk for CKD because of another condition (e.g., diabetes, hypertension, or polycystic kidney) or a solitary kidney. (A solitary kidney can be a congenital or acquired state, with the latter due to nephrectomy for donation or cancer treatment.) Mild-to-moderate CKD is defined as an eGFR of 30 to less than 60 ml per minute per 1.73 m² without substantial proteinuria (<0.3 g of protein per day). Patients with advanced CKD have an eGFR of less than 30 ml per minute per 1.73 m² or substantial proteinuria (>0.3 g per day). Patients transitioning to dialysis therapy usually have good residual kidney function. Protein-energy wasting (PEW) is defined according to the criteria of the International Society of Renal Nutrition and Metabolism.⁶⁶ In the denominator of the dietary recommendations for protein and energy, kg denotes the ideal body weight (IBW), especially for persons with a body-mass index (BMI), the weight in kilograms divided by the square of the height in meters) above 30. The IBW can be estimated in males as 50.0 kg + 2.3 kg for each inch over 5 ft (each 2.5 cm over 152.4 cm) and in females as 45.5 kg + 2.3 kg for each inch over 5 ft. To convert phosphorus to millimoles per day, multiply by .03229. To convert calcium to millimoles per day, multiply by 0.02449. DASH denotes Dietary Approaches to Stop Hypertension.

†† BMI = body mass index.

Kalantar-Zadeh & Foque, Nutritional Management of CKD. *NEJM* Nov 2, 2017

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Challenges of Transition Period from NDD to ESRD

1. Higher mortality
2. Higher costs
3. Best timing?
4. Transition of elderly to ESRD
5. Transition across race/ethnicity
6. Residual kidney function
7. Best format? Incremental vs. abrupt

© K. Kalantar-Zadeh et al. NDT 2017 [Blueprint of TC-CKD]

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Seminars in Dialysis Special Edition May/June 2017

“The Critical Balance – Residual Kidney Function and Incremental Transition to Dialysis”

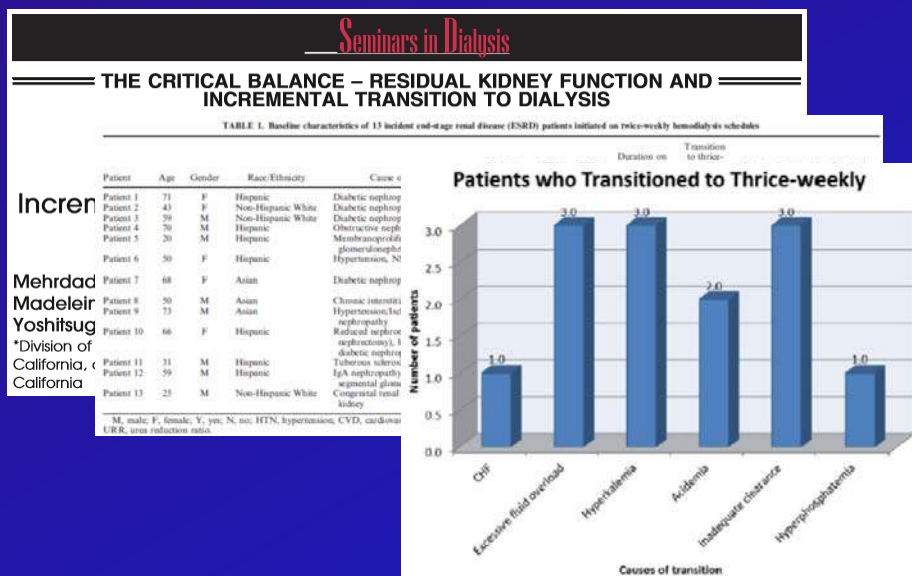
Obi, Chou and Kalantar-Zadeh

Review Paper Title:

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

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The University of California Experience



Ghahremani-Ghajar...Kalantar-Zadeh, Rhee. *Sem Dial* 2017.

66

How to accommodate incremental HD in your dialysis unit?

Patient A: 3x/wk HD

Monday

Wednesday

Friday

Patient B: 3x/wk HD

Tuesday

Thursday

Saturday

Patient A: 2x/wk HD

Monday

Thursday

Patient B: 2x/wk HD

Tuesday

Friday

Patient C: 2x/wk HD

Wednesday

Saturday

Patient A: 2x/wk HD

Monday

Friday

Patient B: 2x/wk HD

Tuesday

Saturday

Patient D: 3x/wk but needs extra HD

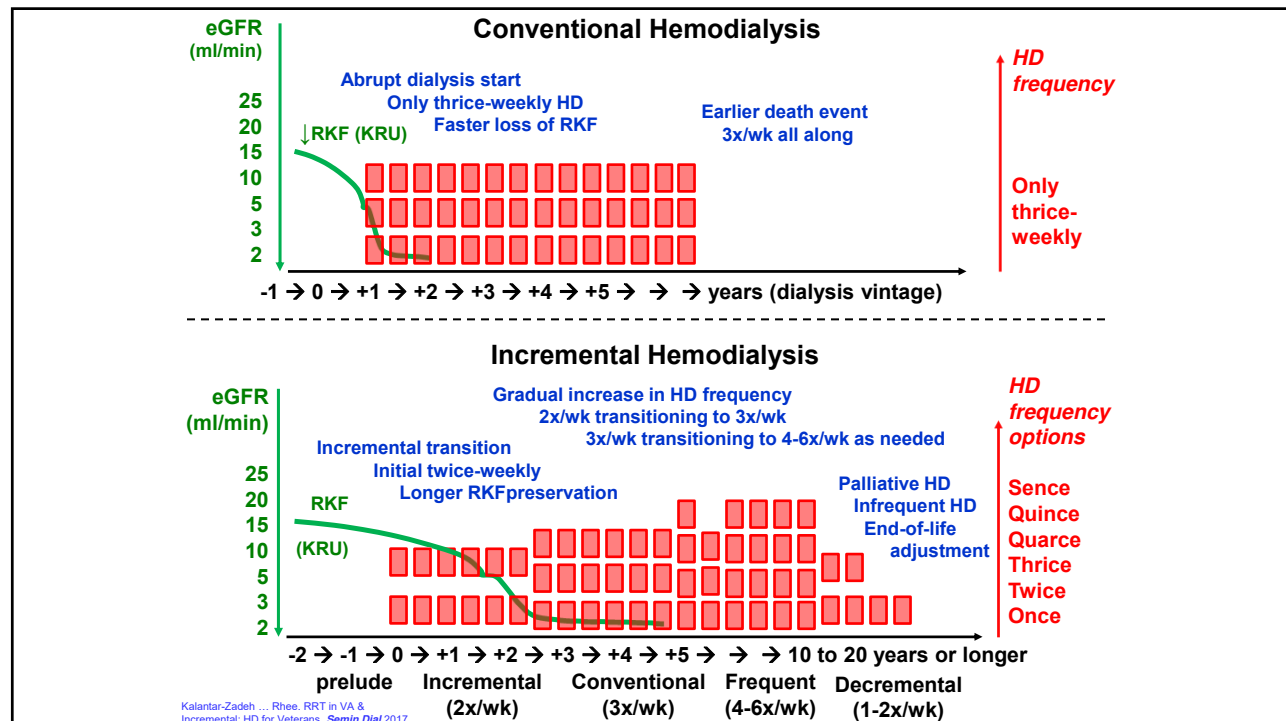
Wednesday

Patient F: 3x/wk but needs extra HD

Thursday

Kalantar-Zadeh ... Rhee. *Semin Dial* 2017.

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Dialysis **Patient-Centeredness** and **Precision Medicine**: Focus on **Incremental Home** Hemodialysis and Preserving Residual Kidney Function

Seminars in Nephrology July 2018

Nieltje Gedney (**Home HD Patients via
Incremental Protocol**)

Kamyar Kalantar-Zadeh

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Table 1: **Types** of incremental dialysis protocols.

Note that in all protocols, residual kidney function needs to be monitored judiciously (monthly to quarterly)

Type of Incremental Dialysis Protocol	Assumption	Suitability
Hemodialysis (HD)		
Type A: Less frequent HD (less than thrice-weekly)*	Maintaining at least 3 to 4 hours of HD treatment time per session	May be more suitable for in-center HD patients
Type B: Shorter HD treatment time (less than 3 hours)	Maintaining at least thrice-weekly HD frequency	Suitable for both in-center and home HD
Type C: Any combination of the above protocols	n/a	Suitable for home and in-center HD.
Peritoneal Dialysis (PD)		
Type D: Shorter total PD dwell time or fluid volume per day	Maintaining daily (7 days a week) PD	Home dialysis
Type E: Less than 7 days a week of PD therapy*	Maintaining standard dwell time and volume	Home dialysis
Type F: Any combination of the above PD protocols	n/a	Home dialysis
Type G: Any combination of PD with sporadic HD sessions	n/a	Combination of home and in-center dialysis

Gedney & Kalantar-Zadeh. *Seminars in Nephrology* July 2018

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Table 2: Precision medicine may allow for greater patient-centeredness of incremental hemodialysis protocols (similar inferences and comments may apply to incremental peritoneal dialysis [PD] comparing less than 7-days-a-week PD versus less dwell time or PD dialysate fill volume).

Patient related aspects	Less frequent HD per week	Shorter HD treatment time	Comments
Smoother transition to dialysis initiation.	+++	++	Once weekly HD may be considered.
Ability to urinate	+++	+++	Any type of incremental dialysis may prolong residual kidney function.
More free-time off dialysis therapy	+++	+	Twice-weekly HD may be a better choice for travelling patients or those far from HD center.
Lower likelihood of cramps, hypotensive episodes or other treatment related symptoms	+	+++	Cramps may also be related to ultrafiltration rate in addition to HD treatment time
Less brisk fluctuation in fluid and electrolytes	+	+++	Twice-weekly HD may lead to larger fluctuations although this is dependent on residual urine output.
Better health-related quality of life and patient satisfaction	+++	++	Less frequent in-center HD vis-à-vis patient transportation and family/care-giver burden
Better suitability for home dialysis therapy	++	+++	Home HD patients may prefer shorter HD treatment times.
Longer preservations of arteriovenous fistula	Gedney & Kalantar-Zadeh. <i>Seminars in Nephrology</i> July 2018		

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Incremental Dialysis going to all nations throughout the world 2014-2019

ISSN 1602-6817 Erscheinungsort: Wien Verlagspostamt: A 8600 Bruck/Mär

Jahrgang 21, Ausgabe 1/19

NEPHRO-NEWS

Forum für Nephrologie und Hypertensiologie



Prof. Dr. med. (Erlangen) Dr. phil. (Berkeley) Kamyar Kalantar-Zadeh, MD, MPH, PhD

Übersetzung: Prof. Dr. Wilfred Druml


Weg zur Präzisionsdialyse:

Inkrementelle Dialyse zur Individualisierung des Dialysebeginns

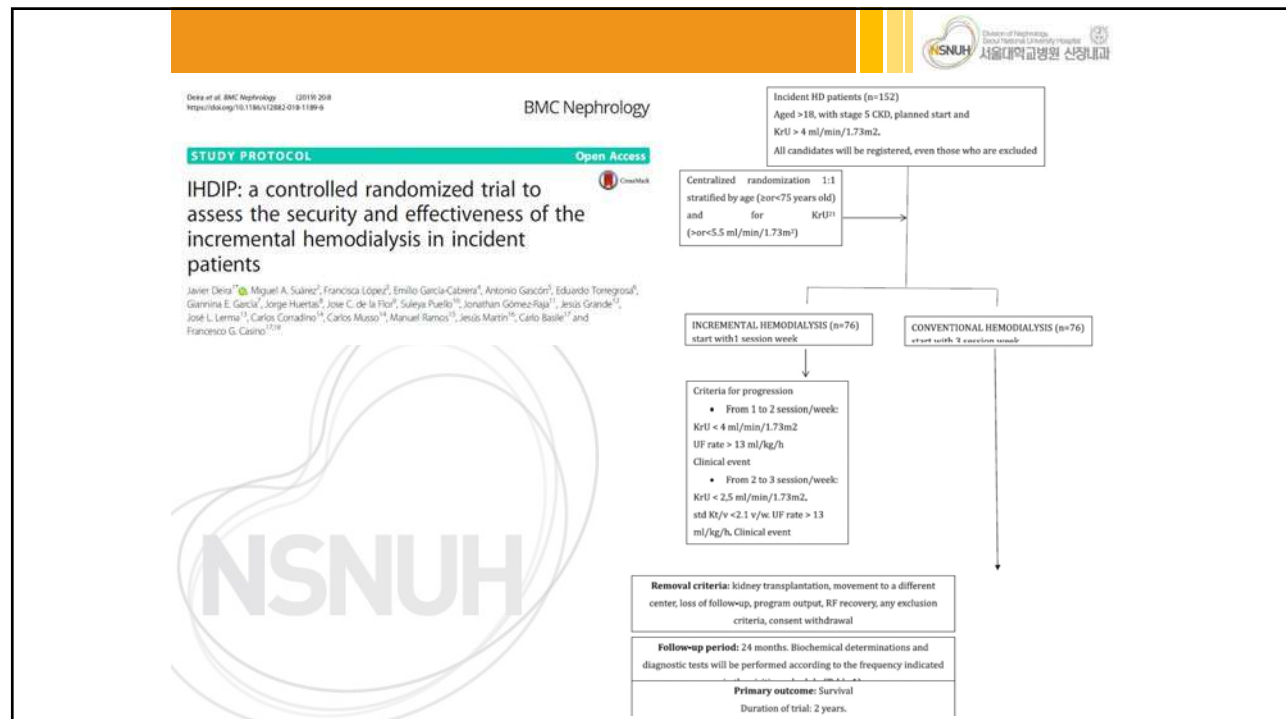
In den letzten Jahren ist die Individualisierung der Betreuung von Patienten mit chronischer Niereninsuffizienz und insbesondere am Übergang in ein chronisches Nierenersatztherapie-Programm ins Zentrum des Interesses gerückt. Dabei hat das



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<div> <div>NIH U.S. National Library of Medicine</div> <div>ClinicalTrials.gov</div> <div>  </div> </div>						
Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1		Recruiting	Individualized Incremental Hemodialysis Study <ul style="list-style-type: none"> 122 participants January 1, 2018 December 2020 Survival (24 mo) 	<ul style="list-style-type: none"> Hemodialysis Complication ESRD Renal Failure 	<ul style="list-style-type: none"> Procedure: Individualized Incremental hemodialysis Procedure: Conventional thrice weekly hemodialysis 	<ul style="list-style-type: none"> Mansoura University Mansourah, Alexandria, Egypt kidney and Urology Center Alexandria, Egypt
2		Recruiting	Incremental Hemodialysis in Incident Patients <ul style="list-style-type: none"> 152 participants March 14, 2018 July 2021 Survival (24 mo) 	<ul style="list-style-type: none"> Renal Disease, End-Stage 	<ul style="list-style-type: none"> Procedure: Incremental haemodialysis Procedure: Conventional haemodialysis 	<ul style="list-style-type: none"> Fundación Sanitaria de Extremadura Mérida, Badajoz, Spain Hospital Virgen del Puerto Plasencia, Cáceres, Spain Hospital San Pedro de Alcántara Cáceres, Spain
3		Recruiting	Incremental Hemodialysis as a Starting Way of Renal Replacement Therapy <ul style="list-style-type: none"> 7 participants April 4, 2017 December 30, 2020 RRF (12mo) 	<ul style="list-style-type: none"> Chronic Renal Failure 	<ul style="list-style-type: none"> Procedure: Incremental hemodialysis Procedure: Conventional hemodialysis 	<ul style="list-style-type: none"> Hospital Ramón y Cajal Madrid, Spain
4		Recruiting	Does Incremental Initiation of Haemodialysis Preserve Native Kidney Function? <ul style="list-style-type: none"> 50 participants January 8, 2018 March 2, 2019 RRF (12 mo) 	<ul style="list-style-type: none"> Kidney Failure Dialysis 	<ul style="list-style-type: none"> Procedure: Standard Haemodialysis Procedure: Incremental dialysis 	<ul style="list-style-type: none"> East and North Hertfordshire NHS Trust (incorporating Mount Vernon Cancer Centre) Stevenage, United Kingdom

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Summary and conclusions: TRANSITION from CKD to twice-weekly HD

- In patients with very-late-stage NDD-CKD the optimal transition of care to kidney replacement therapy is not known.
- Major uncertainty and significant knowledge gaps have persisted pertaining to differential or individualized transitions of care across different age, race and other demographics and dialysis format (frequency, mode, timing, etc.).
- Incremental (**twice-weekly**) hemodialysis may be a superior way to transition from CKD to ESRD in order to **preserve Residual Kidney Function (RKF)** longer, to achieve better quality of life and to save costs and resources.
- Twice-weekly HD may be a better initiation modality for most incident dialysis patients, preserves **Residual Kidney Function (RKF)** longer, and is NOT associated with worse mortality.
- There is an urgent need to examine revival of once- to twice-weekly HD and its implementation in the USA, Americas, Europe, China, India, ... to preserve RKF → there is imminent need for **clinical trials** and more studies on RKF and dialysis frequencies.

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Acknowledgement

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