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KDOQI
Kidney Disease Outcomes Quality Initiative

KDOQI Hemodialysis Adequacy Clinical Practice Guideline Update 2015: What You Need to Know

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Presentation for National Renal Administrators' Association

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Workgroup Disclosure:

All members of the Work Group are required to complete, sign, and submit a disclosure and attestation form showing all such relationships that might be perceived as or actual conflicts of interest. This document is updated annually and information is adjusted accordingly.

Disclosure Statement

Dr. Suri reports no relevant financial relationships.

Outline

- Defining “adequacy”
- Evidence Grading Scale
- Guideline Categories
    1. Timing of Dialysis Inititiation
    2. Frequent and Long Duration Hemodialysis
    3. Measurement of Dialysis: Urea Kinetics
    4. Volume and Blood Pressure Control
    5. Hemodialysis Membranes and Convective Therapies
- Summary of Differences between 2015 Update and 2006
- Discussion

"Adequacy" of Dialysis

- Has traditionally reflected adequacy of small solute clearance
- Thus, these guidelines pertain to the dialysis procedure itself

HOWEVER:

Adequacy of dialysis ≠ adequacy of patient care

- ✓ Optimal patient care entails attention to many aspects other than small solute clearance

  eg. nutrition, anemia, metabolic control, vascular access, diabetes, cardiovascular disease, etc.

- ✓ Quality of life, caregiver burden, and individual patient values and preferences also require consideration

Structure of the Guideline Update

Recommendation Strength

Level 1 **“We recommend”**	Most patients should receive the recommended course of action.
Level 2 **“We suggest”**	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.

Grade of the Evidence

Grade A	**High quality** of evidence. We are confident that the true effect is close to that of the estimate of the effect.
Grade B	**Moderate quality** of evidence. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Grade C	**Low quality** of evidence. The true effect may be substantially different from the estimate of the effect.
Grade D	**Very low quality** of evidence. The estimate of effect is very uncertain and often will be far from the truth.
Ungraded	**Typically included to provide guidance based on common sense, where adequate evidence is lacking.**

Guideline 1: Timing of Hemodialysis Initiation

1.1 Patients who reach **CKD stage 4** (GFR < 30 mL/min/1.73 m^2), including those who have imminent need for maintenance dialysis at the time of initial assessment, should receive **education about kidney failure and options** for its treatment, including kidney transplantation, PD, HD in the home or in-center, and conservative treatment. Patients' family members and caregivers also should be educated about treatment choices for kidney failure. *(Ungraded)*

This is an ungraded statement as there is minimal to no evidence evaluating the value of patient education in this setting; however, the the potential for education and knowledge to improve patient empowerment and autonomous decision-making was recognized by the workgroup.

Guideline 1. Timing of Hemodialysis Initiation

1.2 **The decision to initiate maintenance dialysis** in patients who choose to do so should be based primarily upon an assessment of **signs and/or symptoms associated with uremia**, evidence of protein-energy wasting, and the ability to safely manage metabolic abnormalities and/or volume overload with medical therapy **rather than on a specific level of kidney function** in the absence of such signs and symptoms. *(Ungraded)*

This statement was based primarily on the findings of the IDEAL trial. However, given the controversy in this field, and that the symptoms and signs of the uremic syndrome are ill-defined, this statement was left ungraded.

Observational studies show higher eGFR at dialysis initiation is associated with increased mortality

Table 2. Summary Data From Observational Studies That Assessed the Association Between Serum Creatinine–Based Estimates of Kidney Function at the Time of Initiation of Dialysis and Risk for Death

Study	Sample Size	Study Site	Study Period	Measure of Kidney Function	HR (95% CI) for Association of Kidney Function at Time of Dialysis Initiation With Death Risk
Fink[64] (1999)	5,388	Veterans Affairs, Maryland, USA	04/1995-12/1996	Scr	For every 1-mg/dL higher Scr: 0.96 (0.93-0.99)
Traynor[65] (2002)	235	Glasgow, UK	1987-2000	Cockcroft-Gault CL_{cr}	For every 1-mL/min higher CL_{cr}: 1.11 (1.01-1.21)
Beddhu[66] (2003)	2,920	Dialysis Morbidity and Mortality Study, USA	1996-1997	eGFR by MDRD Study equation	For every 5-mL/min/1.73 m^2 higher eGFR: 1.14 (1.06-1.22)
Kazmi[67] (2005)	302,287	USRDS	1996-1999	eGFR by MDRD Study equation	For eGFR > 10 (reference, <5) mL/min/1.73 m^2: 1.42
Sawhney[68] (2009)	7,299	Canada and Scotland	2000-2005	eGFR by MDRD Study equation	For eGFR > 15 and 10-15 (reference, 5-10) mL/min/1.73 m^2: 1.65 (1.39-1.95) and 1.37 (1.19-1.59), respectively
Stel[69] (2009)	6,716	Europe	2003	eGFR by MDRD Study equation	For every 1-mL/min/1.73 m^2 higher eGFR: 1.02 (1.01-1.04)
Evans[70] (2011)	901	Sweden	05/1996-05/1998	eGFR by MDRD Study equation	For eGFR > 7.5 (reference: <7.5) mL/min/1.73 m^2: 0.84 (0.64-1.10)
Hwang[71] (2010)	23,551	Taiwan	07/2001-12/2004	eGFR by MDRD Study equation	For quintile 5 eGFR (>6.52 mL/min/1.73 m^2) (reference, quintile 1, <3.29 mL/min/1.73 m^2): 2.44 (2.11-2.81)
Lassalle[72] (2010)	11,685	France	2002-2006	eGFR by MDRD Study equation	For every 5-mL/min/1.73 m^2 higher eGFR: 1.09 (1.05-1.14)
Wright[73] (2010)	895,293	USRDS	01/1995-09/1996	eGFR by MDRD Study equation	For eGFR > 15 and 10-15 (reference, 5-10) mL/min/1.73 m^2: 1.44 (1.43-1.45) and 1.15 (1.15-1.16), respectively
Grootendorst[74] (2011)	569	Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)	1997-2005	eGFR by MDRD Study equation	For highest tertile of eGFR (reference: lowest tertile): 1.4 (1.0-1.9)
Rosansky[75] (2011)	81,176	USRDS (nondiabetics, aged 45-64 y)	1995-2006	eGFR by MDRD Study equation	For eGFR > 15.0 and 10.0-14.9 (reference, < 5) mL/min/1.73 m^2: 1.74 and 1.47, respectively
Crews[76] (2014)	84,654; propensity-matched: 61,930	USRDS (aged ≥ 67 y, ≥2 y of prior Medicare coverage)	2006-2008	eGFR by MDRD Study equation	For eGFR ≥ 10 (reference, <10) mL/min/1.73 m^2: 1.11 (1.08-1.14) for propensity-matched analyses
Crews[77] (2014)	652 (187 initiating dialysis)	Cleveland Clinic	2005-2009	eGFR by MDRD Study equation	For eGFR ≥10 (reference, <10) mL/min/1.73 m^2: OR, 0.85 (0.65-1.11) for inverse probability–weighted analyses
Jain[78] (2014)	8,047 initiating PD	Canadian Organ Replacement Register	2001-2009	eGFR by MDRD Study equation	For eGFR > 10.5 and 7.5-10.5 (reference, <7.5) mL/min/1.73 m^2: adjusted HRs of 1.08 (0.96-1.23) and 0.96 (0.86-1.09), respectively

Abbreviations: CI, confidence interval; CL_{cr}, creatinine clearance; eGFR, estimated glomerular filtration rate; HR, hazard ratio; MDRD, Modification of Diet in Renal Disease; OR, odds ratio; PD, peritoneal dialysis; Scr, serum creatinine; UK, United Kingdom; USA, United States; USRDS, US Renal Data System.

However, higher residual kidney clearance at dialysis initiation is NOT associated with increased mortality

Table 3. Summary Data From Observational Studies That Assessed the Association Between Measured Kidney Function at the Time of Initiation of Dialysis and Risk for Death

Study	Sample Size	Study Site	Study Period	Measure of Kidney Function	HR (95% CI) for Association of Kidney Function at Time of Dialysis Initiation With Death Risk
Bonomini[79] (1985)	340	Single Italian center		CL_{cr}	12-y survival in early dialysis group: (mean CL_{cr}, 12.9 mL/min), 77%; late dialysis group (mean CL_{cr}, 2.1 mL/min): 51%; no adjustment made for differences in patient characteristics
Tattersal[80] (1995)	63	Single UK center	1991-1992	Renal Kt/V_{urea}	Mean renal Kt/V_{urea} lower in 6 individuals who died; no adjustment made for differences in patient characteristics
Churchill[81] (1997)	680	Canadian-USA Study on Adequacy of Peritoneal Dialysis (CANUSA)	9/1990-12/1992	24-h mean of urinary urea clearance and CL_{cr}	For every 5-L/wk higher mGFR: 0.95 (0.91-0.99)
Beddhu[66] (2003)	1,072	Dialysis Morbidity and Mortality Study, USA	1996-1997	Assumed 24-h urinary CL_{cr}	For every 5-mL/min higher CL_{cr}: 0.98 (0.86-1.14)
Grootendorst[74] (2011)	569	Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)	1997-2005	24-h mean of urinary urea clearance and CL_{cr}	Highest tertile of mGFR (reference: lowest tertile of mGFR): 1.0 (0.7-1.3)

Abbreviations: CI, confidence interval; CL_{cr}, creatinine clearance; HR, hazard ratio; mGFR, measured glomerular filtration rate; UK, United Kingdom; USA, United States.

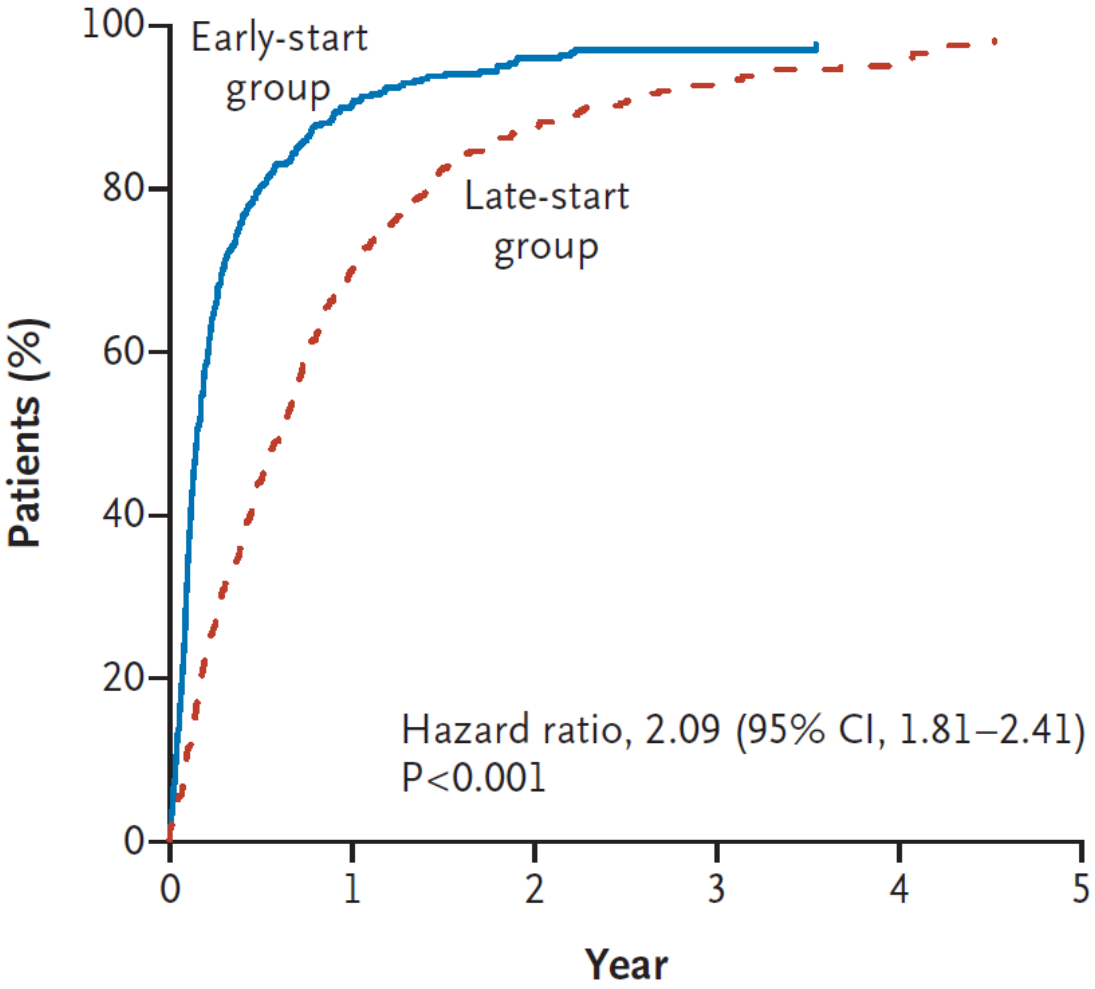
IDEAL Randomized Controlled Trial

Cooper et al, NEJM, 363:609-619, 2010

- 32 centers in Australia/NZ
- **828 patients** with CrCl 10-15 ml/min/1.73 m2
- Randomized to start HD early (CrCl = 10-14) vs. late (CrCl = 5-7).
- High crossover rate:
  - **19% earlies started late; 76% of lates started early**
  - as treated CrCl values were 12.0 vs. 9.8 (eGFR 9.0 vs. 7.8).
- **There were no observed differences in mortality** (primary outcome) **or in secondary outcomes** (cardiovascular events*, infectious events, complications of dialysis, cost, nutritional status, quality of life, cardiac structure or function).

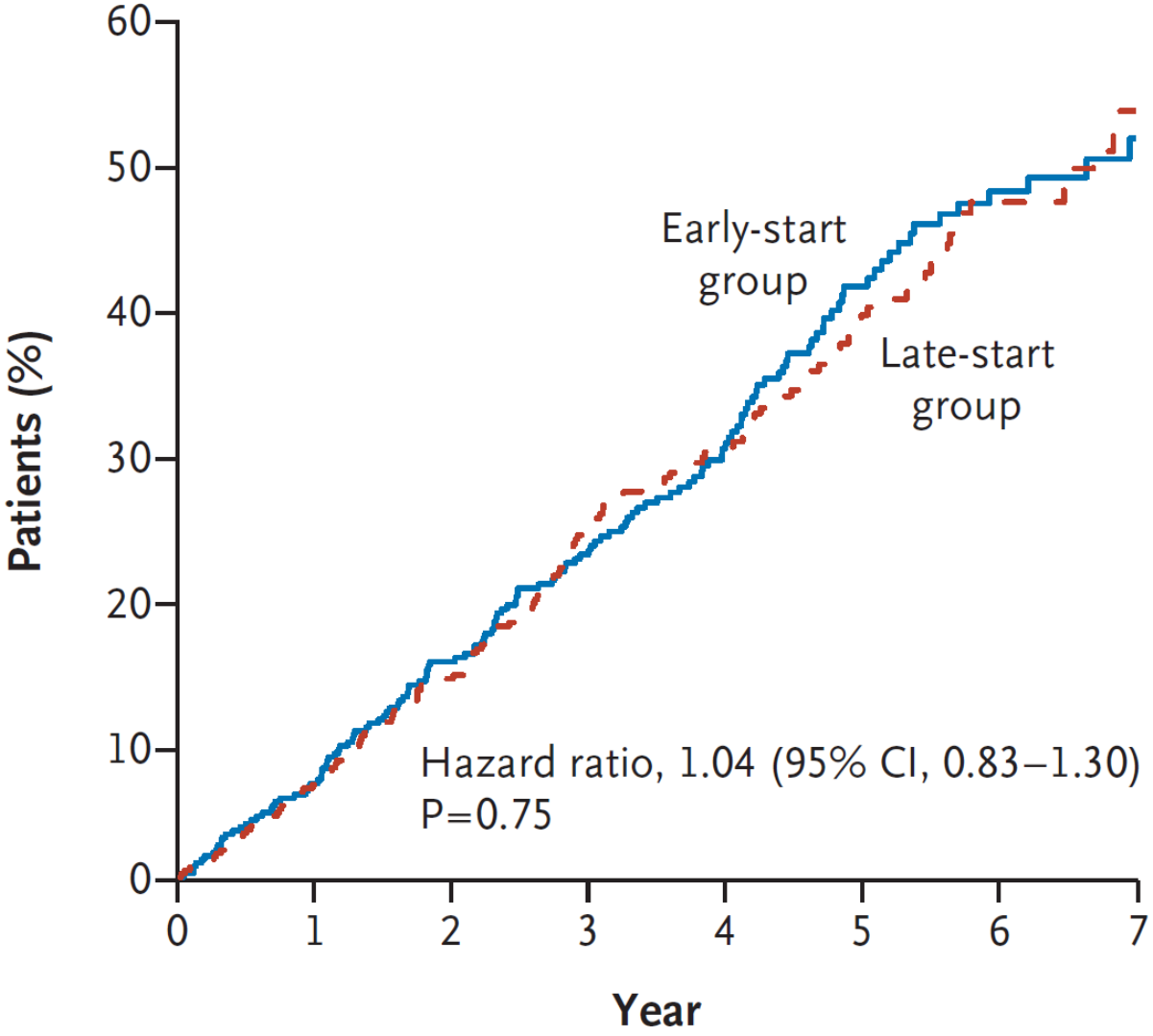
*CV death, nonfatal MI, nonfatal stroke, Transient ischemic attack, new angina

IDEAL Study: Time to Start of Dialysis



No. at Risk						
Early start	404	35	12	8	2	1
Late start	424	118	45	21	9	3

IDEAL Study: Time to Death



No. at Risk

Early start	404	358	305	249	177	99	59	32
Late start	424	385	333	254	187	115	60	32

Guideline 2: Frequent and Long Duration HD

In-center Frequent Hemodialysis

2.1 **We suggest** that patients with end-stage kidney disease be offered in-center short frequent hemodialysis as an alternative to conventional in-center thrice weekly hemodialysis after considering **individual patient preferences, the potential quality of life and physiological benefits, and the risks** of these therapies. *(2C)*

2.2 **We recommend** that patients considering in-center short frequent hemodialysis be informed about the risks of this therapy, including a possible **increase in vascular access procedures** *(1B)* and the potential for **hypotension during dialysis**. (1C)

Guideline 2: Frequent and Long Duration HD

Home Long Hemodialysis

2.3 **Consider** home long hemodialysis (6-8 hours, 3 to 6 nights per week) for patients with end-stage kidney disease who prefer this therapy for lifestyle considerations. *(Ungraded)*

2.4 **We recommend** that patients considering frequently administered home long hemodialysis be informed about the risks of this therapy, including possible **increase in vascular access complications**, **potential for increased caregiver burden**, and **accelerated decline in residual kidney function**. *(1C)*

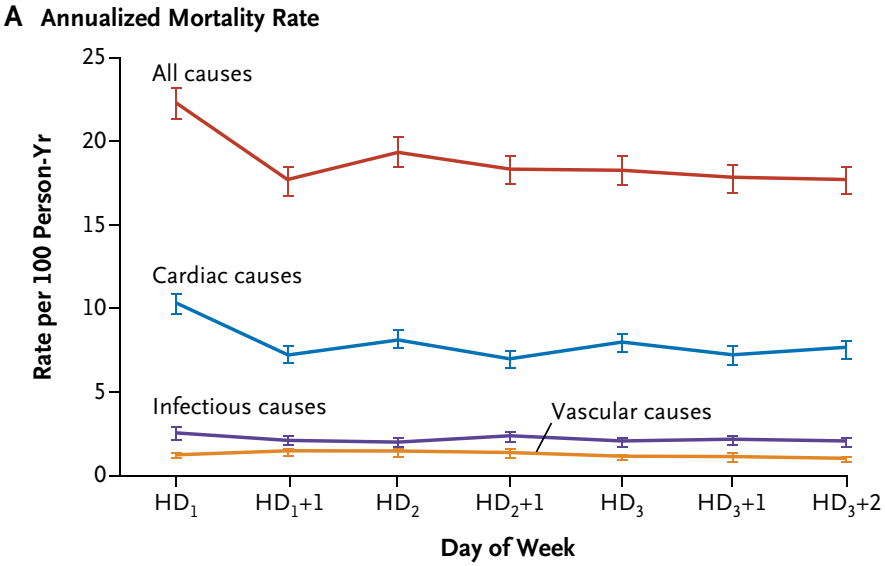
2.5 **During pregnancy,** women with end-stage kidney disease should receive **frequent long hemodialysis** either in-center or at home, depending on convenience. *(Ungraded)*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long Interdialytic Interval and Mortality among Patients Receiving Hemodialysis

Robert N. Foley, M.B., David T. Gilbertson, Ph.D., Thomas Murray, M.S., and Allan J. Collins, M.D.



Daily Variation in Death in Patients Treated by Long-term Dialysis: Comparison of In-Center Hemodialysis to Peritoneal and Home Hemodialysis

Rathika Krishnasamy, MD,[1,2] Sunil V. Badve, MD,[1,2] Carmel M. Hawley, M Med Sci,[1,2] Stephen P. McDonald, PhD,[1,3] Neil Boudville, M Med Sci,[1,4] Fiona G. Brown, PhD,[1,5] Kevan R. Polkinghorne, PhD,[1,5] Kym M. Bannister, MD,[1,3] Kathryn J. Wiggins, PhD,[1,6] Philip Clayton, MM Clin Epi,[1,7,8] and David W. Johnson, PhD[1,2]

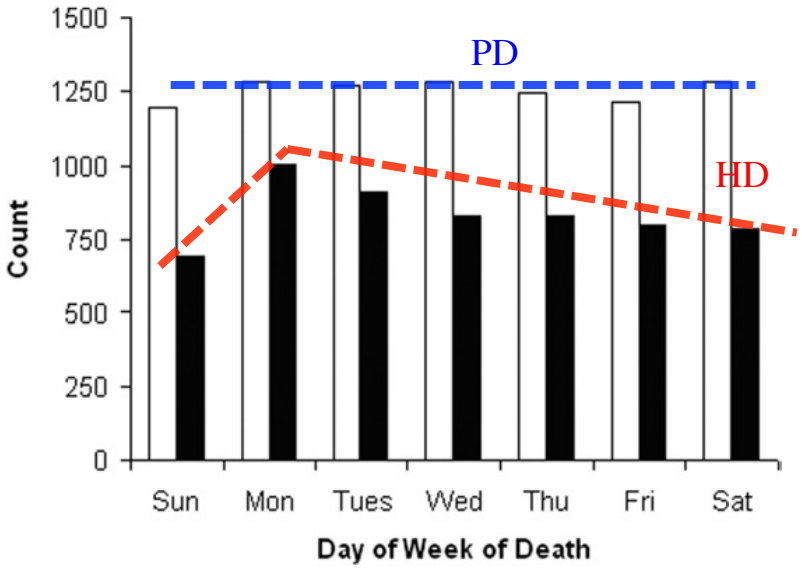
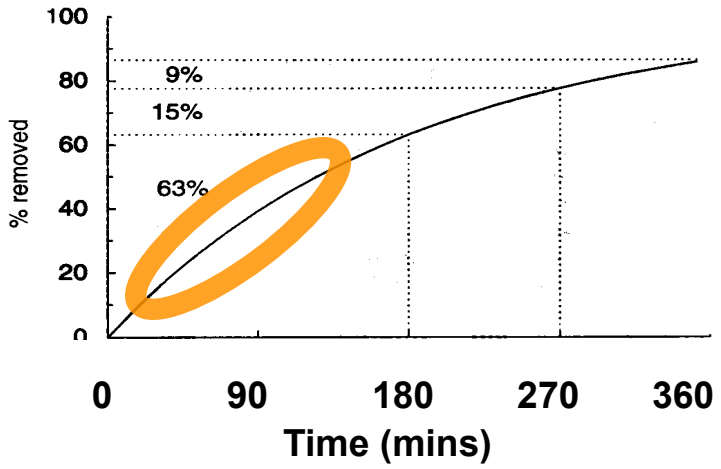
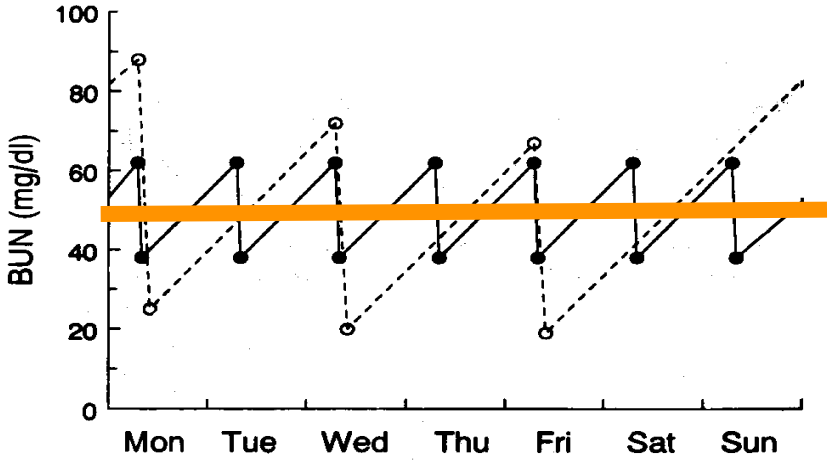


Figure 2. Occurrence of cardiac deaths in 10,338 hemodialysis (HD; black bars) and 4,298 peritoneal dialysis (PD; white bars) patients in Australia and New Zealand in 1999-2008, according to the day of the week of death.

Physiological Rationale for Frequent and Long HD

- greater weekly small solute clearance as more time spent on the "steepest part" of removal curve
- decreased fluctuations in solute concentrations ...less "uremia"?
- greater ease of ultrafiltration .....better volume/ BP control, ↓symptoms
- greater clearance of phosphate and beta-2M, whose removal is time dependent..... ....improved CV outcomes?





Depner TA et al, as reproduced in:
Suri RS and Kilger AS: Frequent Hemodialysis, in Chronic Kidney Disease, Dialysis, and Transplantation (3rd ed.), Himmelfarb J and Sayegh MH (editors), pp. 370-384, 2010.

Frequent Hemodialysis Network (FHN) randomized trials: Study design

- DAILY TRIAL (N=245)
  - in-center daily HD 1.5-2.75 hrs 6 d/wk OR In-center conventional HD
- NOCTURNAL TRIAL (N=87)
  - home nocturnal HD >6 hrs 6 days/wk OR home conventional HD

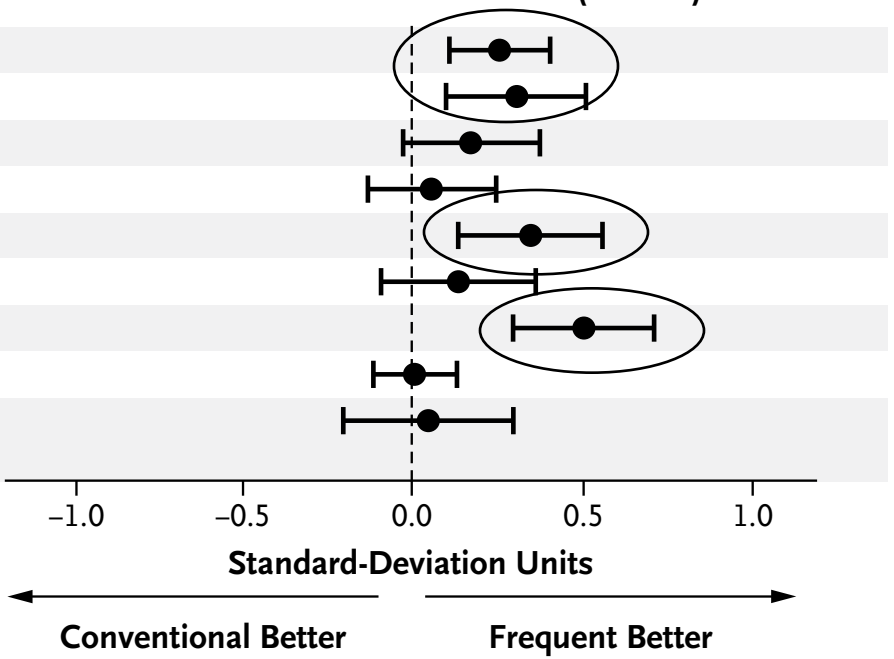
- Follow-up 1 year
- 2 co-primary outcomes: 1) LV mass or death 2) QOL or death
- Several secondary and safety outcomes, not powered for hard outcomes

Suri RS et al, Kidney Int 71(4):349-59, 2007.

FHN Daily Trial RESULTS (n=245)

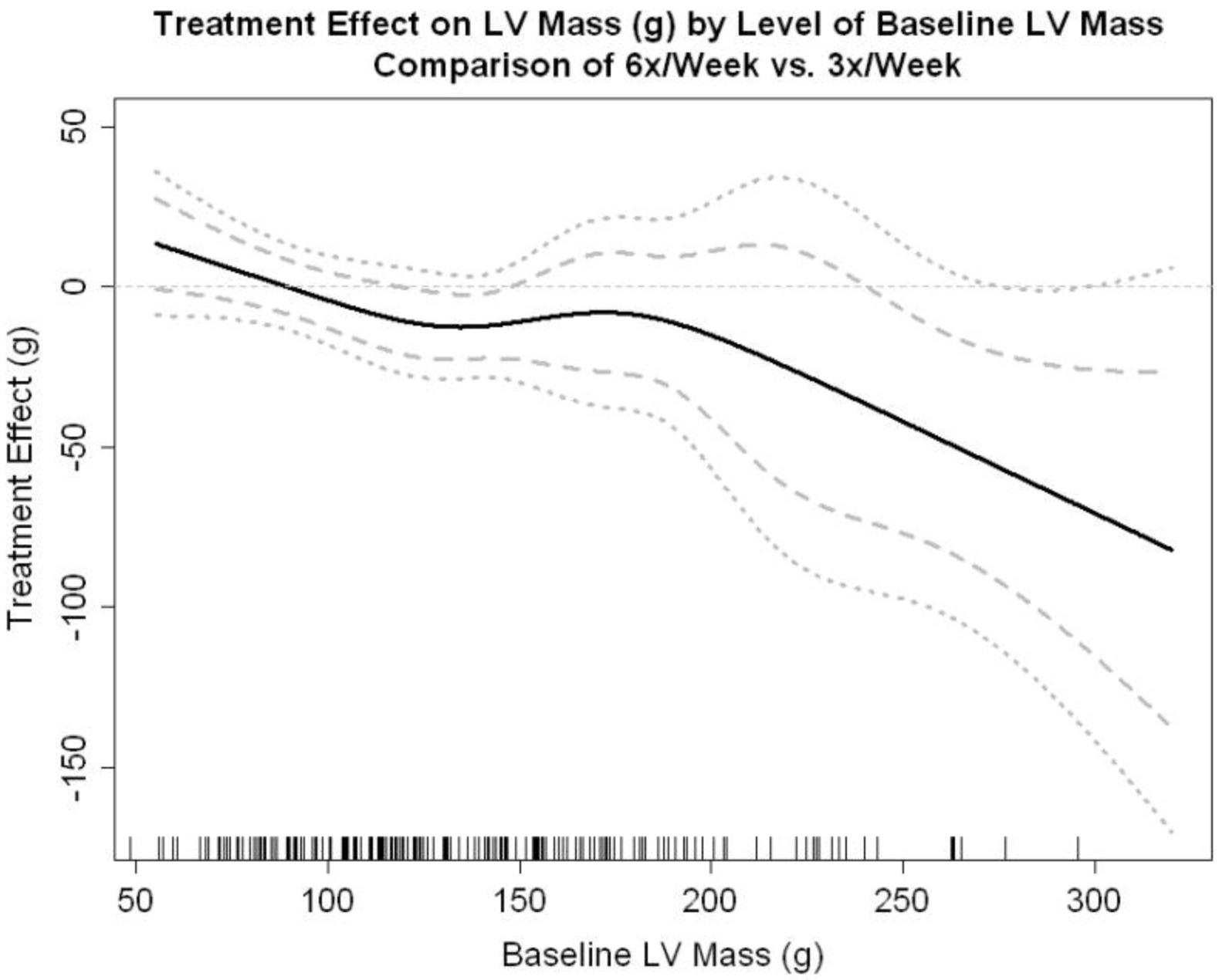
C Main Secondary Outcomes

Outcome	Effect Measure
LV mass	Mean decrease
Physical-health composite score	Mean increase
Beck Depression Inventory score	Mean decrease
Predialysis albumin	Mean increase
Predialysis phosphorus	Mean decrease
ESA dose	Mean decrease in log
Predialysis systolic blood pressure	Mean decrease
Trail Making Test Part B	Negative log relative risk
Death or hospitalization unrelated to vascular access	Negative log hazard ratio



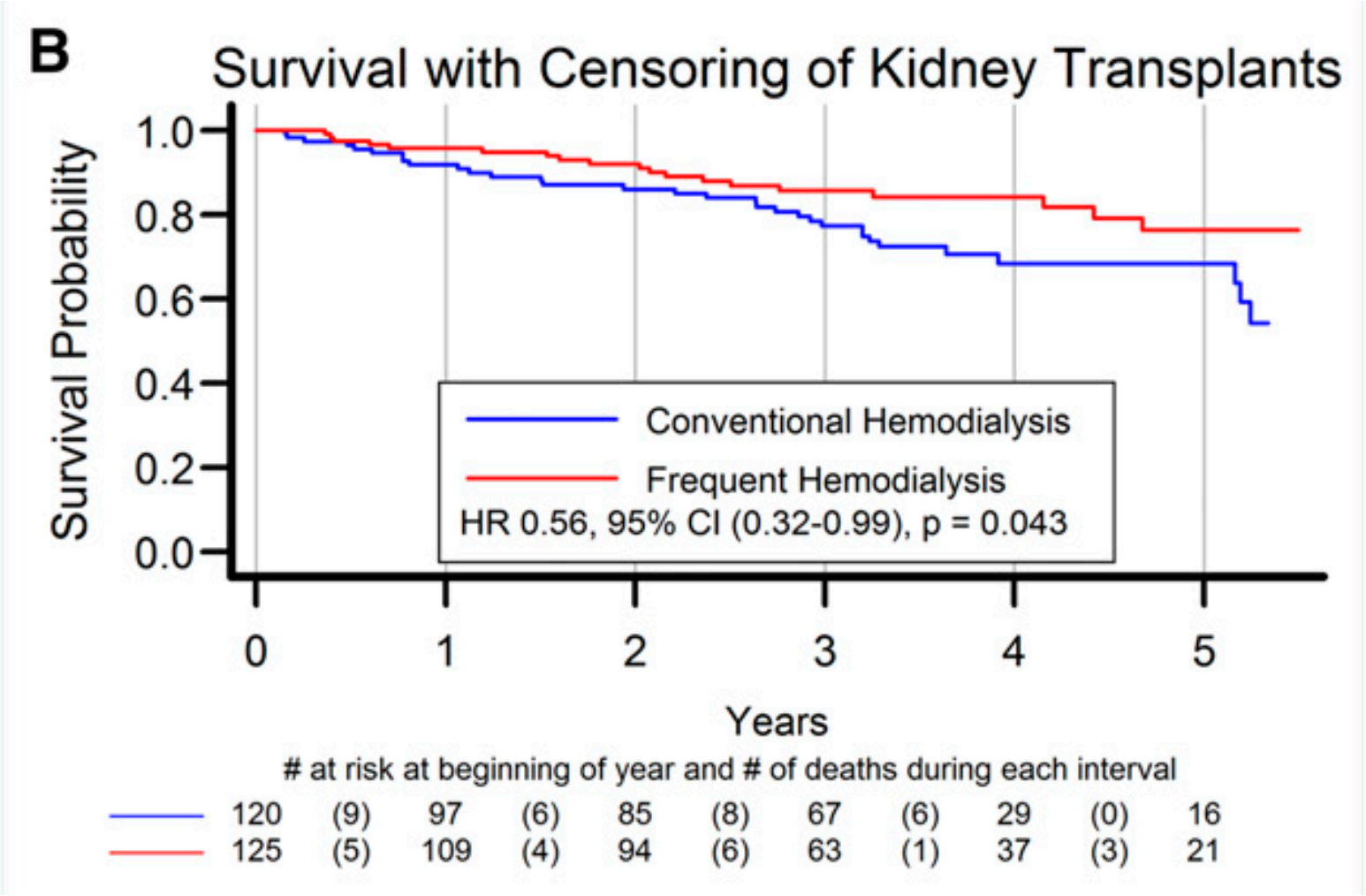
- Daily HD improved quality of life, left ventricular mass index, blood pressure, and pre-dialysis phosphorus.

FHN Trial Group. NEJM 363(24): 2287-300, 2010

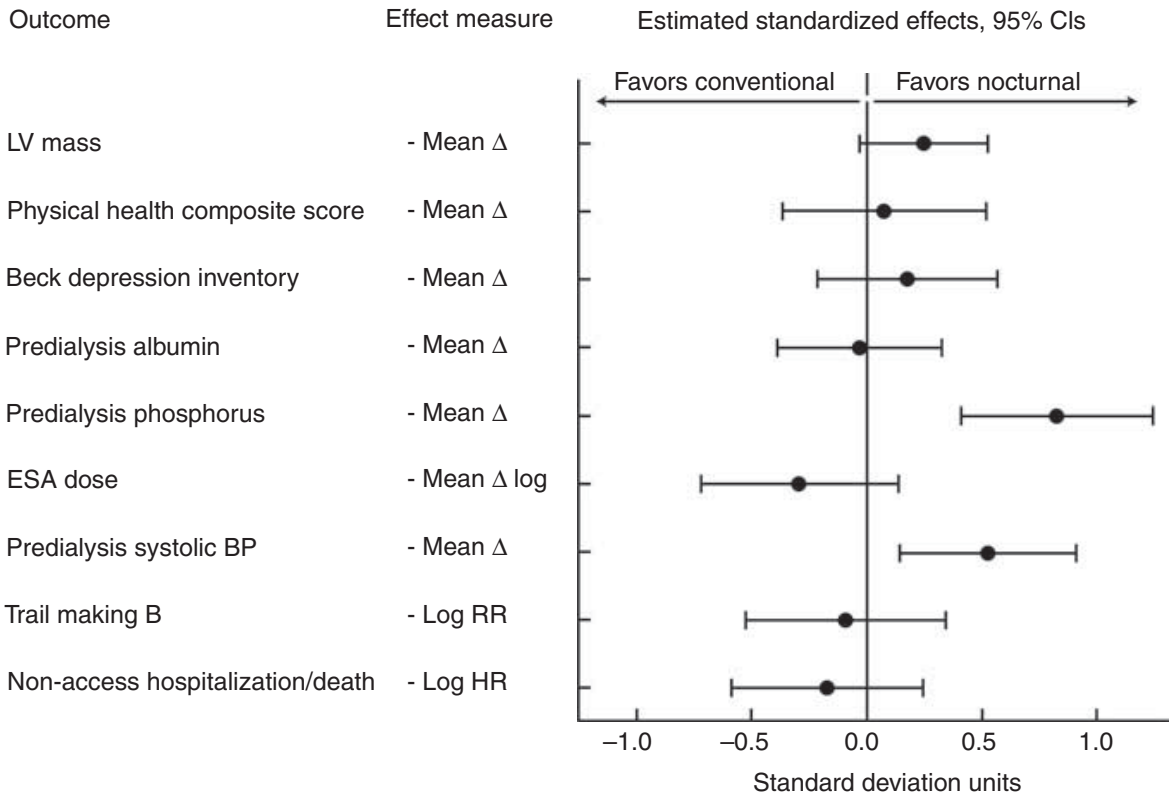


Chan CT et al. Circ Cardiovas Imaging 2012

Survival: FHN Daily Trial



FHN Nocturnal Trial RESULTS (n=87)



- Nocturnal trial largely negative, underpowered.
- No change in QOL.
- Some improvements in blood pressure, and pre-dialysis phosphorus.

FHN Trial Group. Kidney International 80(10): 1080-91, 2011

Alberta Nocturnal Trial RESULTS (n=51)

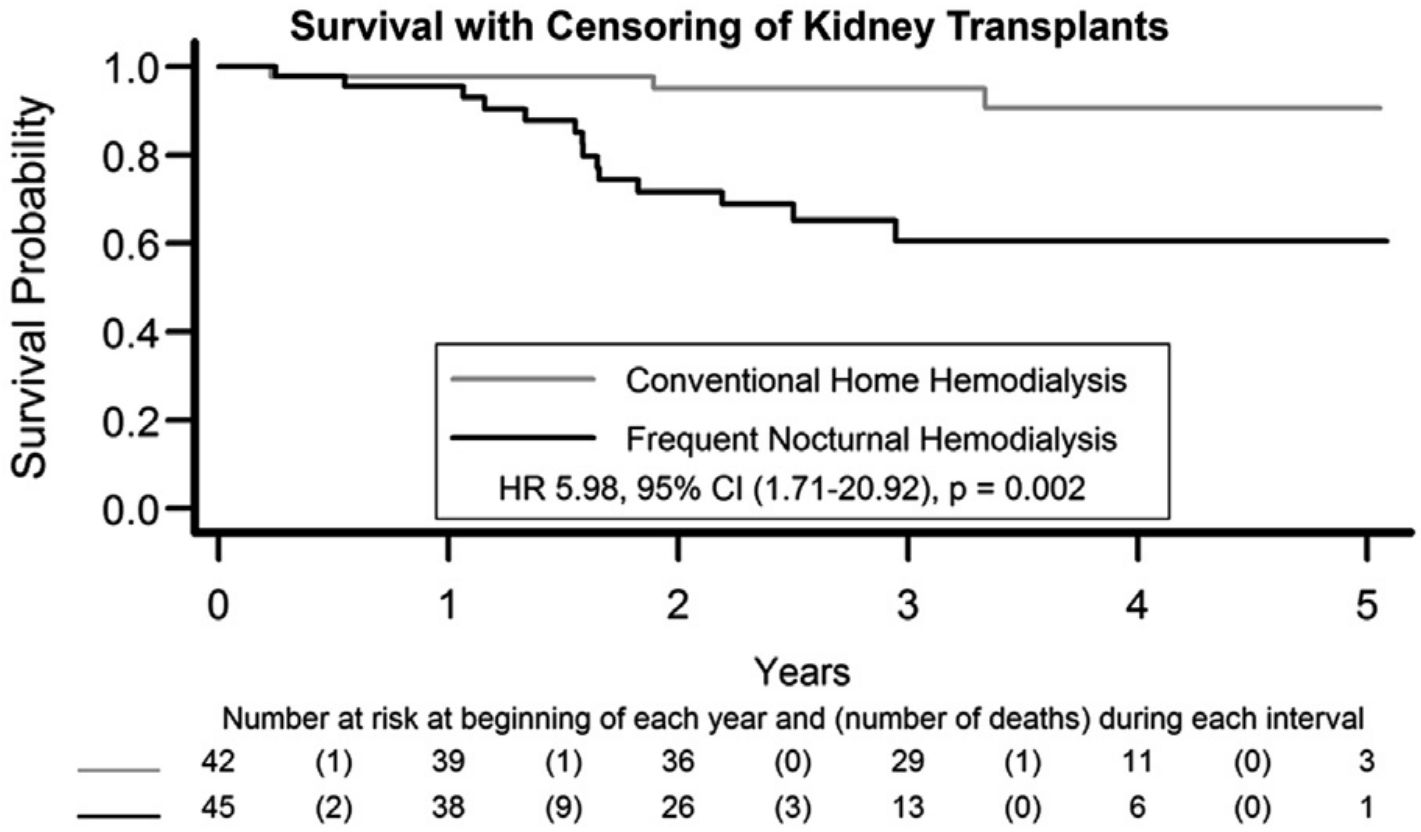
Table 2. Outcomes for LV Mass, Blood Pressure, Anemia, and Mineral Metabolism[a]

Characteristic	Nocturnal Hemodialysis[b] (n = 26)	Conventional Hemodialysis[b] (n = 25)	Between-Group Comparison (95% CI)[c]
LV mass, mean (SD), g			
Baseline	177.4 (51.1)	181.5 (92.3)	–4.1 (–49.5 to 41.3)
Exit	163.6 (45.2)	183.0 (84.2)	–19. 4 (–60.5 to 21.7)
Change	–13.8 (23.0)	1.5 (24.0)	–15.3 (–29.6 to –1.0)[d]
LV mass, mean (SD), g/m^2			
Baseline	92.4 (26.6)	101.8 (50.6)	–9.4 (–34.0 to 15.2)
Exit	85.3 (23.2)	102.8 (46.1)	–17. 5 (–39.8 to 4.6)
Change	–7.1 (12.4)	1.0 (14.1)	–8.1 (–16.2 to –0.1)[d]

- Nocturnal HD improved LV mass, BP, and phosphate, but not quality of life or anemia.

Culleton et al, JAMA 298(11); 1291 -1299, 2007

Survival: FHN Nocturnal Trial



Vascular access complications were increased with frequent HD in the FHN trials

- Primary composite outcome: time to 1st
  - ✧ Access repair = any procedure carried out on the access
  - ✧ Access loss = anytime a NEW access was required (this included catheter rewires but did NOT include elective catheter removals)
  - ✧ Access-related hospitalisation

Suri RS et al, JASN, Mar 2013

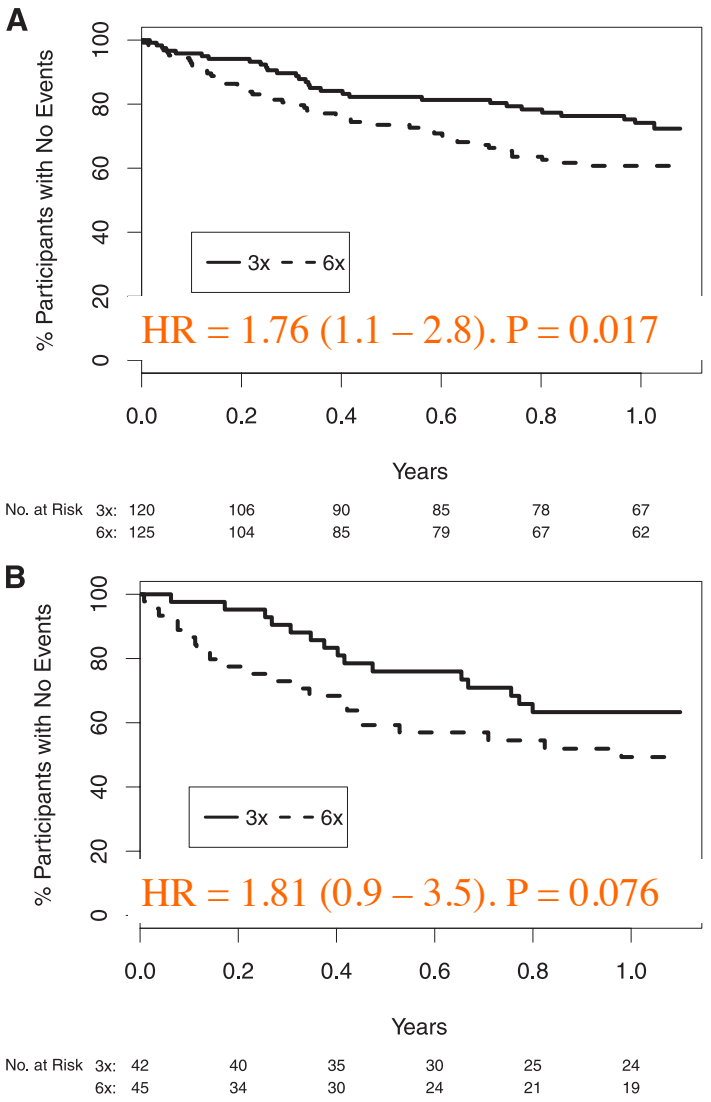
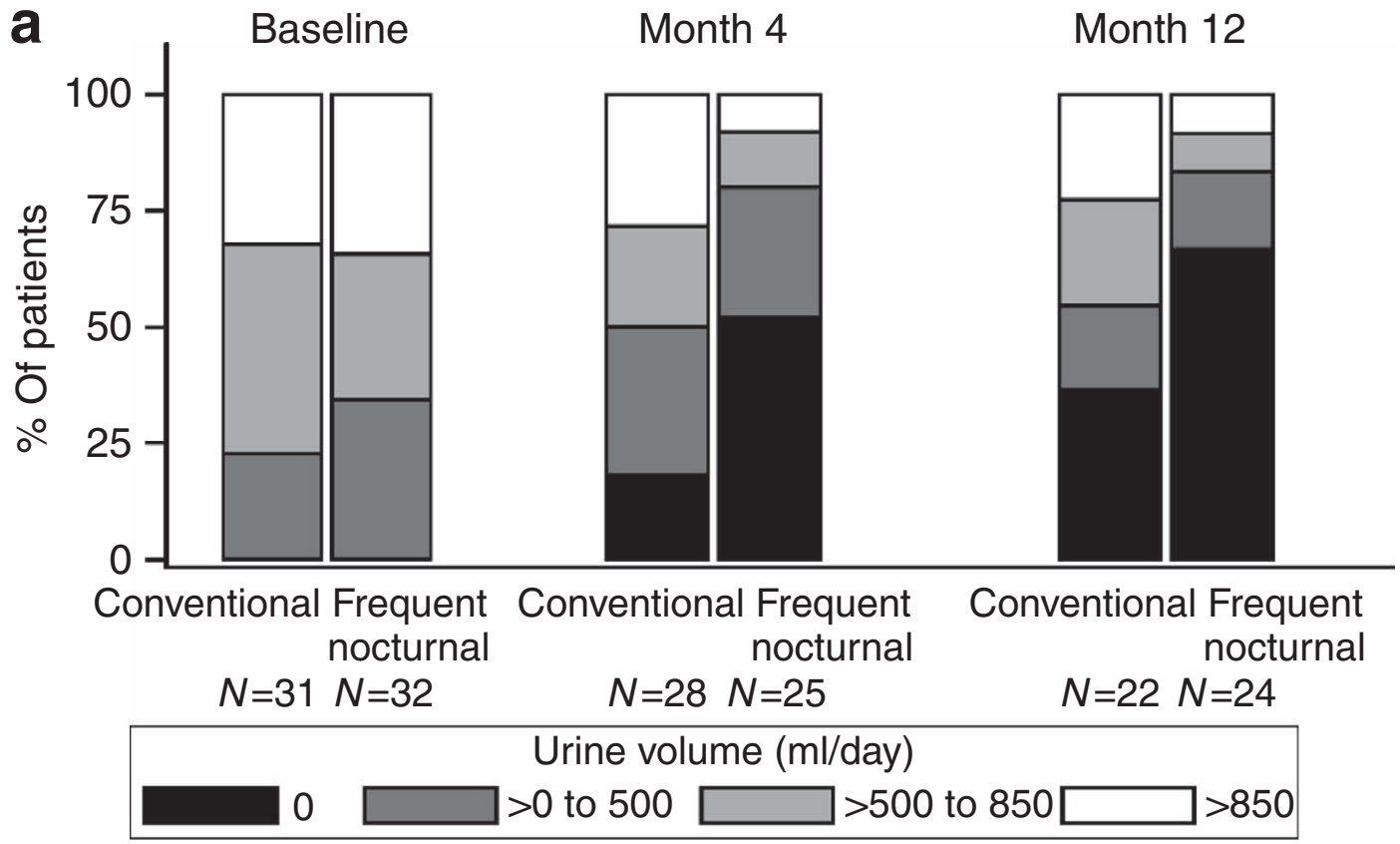


Figure 1. Kaplan-Meier curves of time to first access repair, access loss, or access hospitalization. (A) Daily Trial. (B) Nocturnal Trial.

Nocturnal HD resulted in accelerated loss of residual kidney function



Daugirdas JT et al, Kidney Int. 2013;83(5):949-58.

Table 2: Cousineau Perceived Burden Scores Over Time

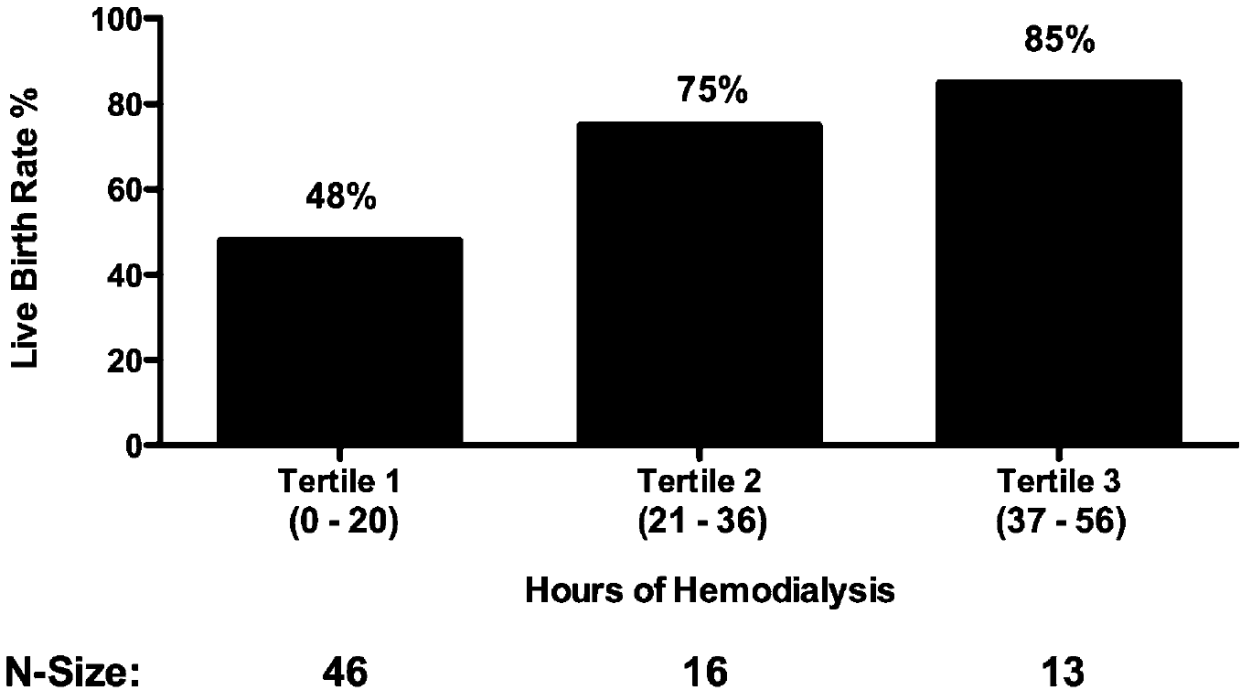
	3 times per week	6 times per week	Between group difference*	p-value
DAILY				
Month 4	– 1.1 ± 2.8	–2.7 ± 2.5	–1.6 (–8.4, 5.2)	0.64
Month 12	–2.6 ± 3.1	–4.7 ± 2.7	–2.1 (–9.4, 5.3)	0.58
NOCTURNAL				
Month 4	–0.3 ± 2.6 –2.8 ± 2.8	+5.9 ± 2.8 +9.6 ± 3.0	+6.2 (–0.8, 13.3) 9.8 (2.4, 17.3)	0.083 0.0093
Month 12	–5.7 ± 2.7 –5.4 ± 3.1	+0.5 ± 2.7 +4.0 ± 3.4	+6.1 (–0.8, 13.1) 9.4 (0.55, 18.3)	0.084 0.038

- There was NO increased perceived caregiver burden with daily HD.
- There was a increased perceived caregiver burden with nocturnal HD at home.

Suri RS et al, CJASN 2014:9(5):936-42.

Long frequent versus standard dialysis during pregnancy: Canadian Study

Source	N	Dialysis Hrs/wk	Pregnancy Duration	Birth rate	Birth wt (g)
Canada	22	43 ± 6	36 wks	86.4%	2118 ± 857
USRDS	70	17 ± 5	27 wks	61.4%	1748 ± 949



Hladunewich MA, et al:
JASN 25(5):1103-9, 2014

Guideline 3: Measurement of Dialysis: Urea Kinetics

3.1 We recommend a **target single pool Kt/V (spKt/V) of 1.4** per hemodialysis session **for patients treated thrice weekly**, with a **minimum delivered spKt/V of 1.2**. *(1B)*

3.2 In patients with significant **residual native kidney function** (Kr), **the dose of hemodialysis may be reduced provided Kr is measured periodically**. *(Ungraded)*

3.3 For hemodialysis schedules other than thrice weekly, a target standard Kt/V of 2.3 volumes per week with a minimum delivered dose of 2.1 using a method of calculation that includes the contributions of ultrafiltration and residual kidney function. *(Ungraded)*

- **National Cooperative Dialysis Study** (NCDS, NEJM 1981) randomized 151 patients to high vs. low urea concentration and short vs. long time
- Re-analysis of the NCDS that Kt/V 0.8 better than Kt/V 0.4

Table 2. NCDS Data (12)

Group	Time	Target TAC urea* (mg/dL)	Achieved TAC urea* (mg/dL) (±SEM)	~URR †	~Kt/V ‡	Midweek predialysis BUN (mg/dl) (±SEM)	Medical withdrawal rate at 1 year (%)	Non-hospitalized at 1 year (%)
I	4:29 ± 0:03	50	51.3 ± 1.1	0.57	0.85	71.2 ± 1.4	18	86
II	4:30 ± 0:03	100	87.7 ± 1.4	0.35	0.47	104.9 ± 1.7	45	46
III	3:19 ± 0:03	50	54.1 ± 1.1	0.55	0.80	73.1 ± 1.4	6	69
IV	3:14 ± 0:03	100	89.6 ± 1.2	0.30	0.45	109.1 ± 1.5	62	31

For medical withdrawal rates: $p < 0.0001$ for effect of TAC urea; $p > 0.05$ for effect of TIME. For hospitalization: $p < 0.0001$ for effect of TAC urea; $p = 0.06$ for effect of TIME

*To convert BUN to mmol/L, divide by 2.8

† Kt/V approximations assume a nPNA of 1.0 g/kg/day (which was the mean nPNA achieved in NCDS). For nPNA range of 0.6–1.2 the estimated Kt/V range is as follows: for groups I and III, Kt/V range is 0.4–1.05; for groups II and IV, Kt/V range is 0.2–0.6 (64)

‡ URR approximations assume ultrafiltration and urea generation rate of 0 (69)

Suri RS, Blake PG. "*Adequacy of Hemodialysis*" in: Replacement of Renal Function by Dialysis, (5th edition), Horl W et al (editors), Pp 597-638, 2004.

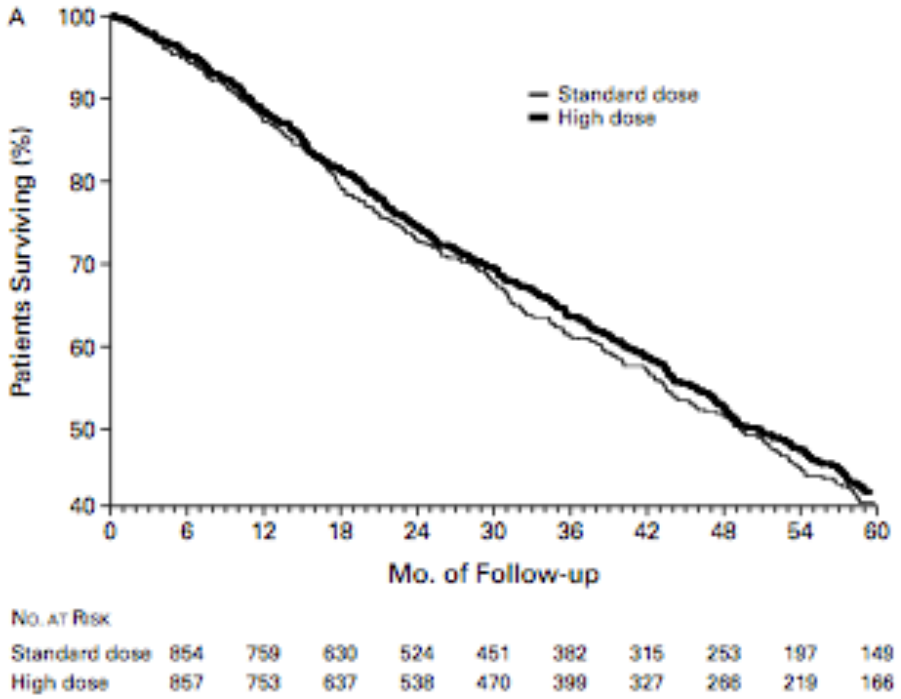
How much dialysis is enough? - HEMO study

- After the NCDS, numerous observational studies suggested that higher urea clearances are associated with high mortality on thrice weekly HD

- HEMO Study[1] randomized patients to eKt/V 1.0 vs. 1.4: NO CHANGE IN MORTALITY.

- eKt/V of 1.0 is approximately equal to spKt/V of 1.2

- Target spKt/V of 1.4 ensures that <10% of treatments are spent <1.2



[1]Eknoyan G, et al. New Engl J Med 347(25): 2010-19, 2002

- Treatment of the patient should not stop after achieving an "adequate" Kt/V_{urea}. Nor is target small solute clearance the only factor which should be considered during dialysis.
- Frequency and treatment time should be individualized considering small solute clearance, residual renal function, quality of life, predicted life-span, and patient values.
- Patients with significant residual function may not require 3 full treatments per week, and thus the dose of dialysis may be reduced. Conversely, other patients may require more frequent or longer treatments.
- Recommendations on how to measure pre- and post-dialysis urea have not changed:

  -predialysis: draw before injecting heparin, saline, or other potential diluents

  -post-dialysis: draw blood from the dialyzer inflow port after slowing blood flow to 100ml/min for 15 secs OR after stopping dialysate flow for 3 mins

Guideline 4. Volume and BP Control: Treatment Time and Ultrafiltration Rate

4.1 **We recommend** that patients with low residual kidney function (< 2 ml/min) undergoing thrice weekly hemodialysis be prescribed **a bare minimum of three hours per session**. *(1D)*

4.1.1 **Consider longer hemodialysis treatment times** or additional hemodialysis sessions for patients with large interdialytic weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, or poor metabolic control (such as hyperphosphatemia, metabolic acidosis, and/or hyperkalemia). *(Ungraded)*

Guideline 4. Volume and BP Control: Treatment Time and Ultrafiltration Rate

4.2 **We recommend** both reducing **dietary sodium intake** as well as **adequate sodium/water removal** with hemodialysis to manage hypertension, hypervolemia, and left ventricular hypertrophy. *(1B)*

4.2.1 Prescribe an ultrafiltration rate for each hemodialysis session that allows for an optimal balance among achieving euvolemia, adequate blood pressure control and solute clearance, while minimizing hemodynamic instability and intradialytic symptoms. *(Ungraded)*

Guideline 4. Volume & BP Control

•Strong recommendation to minimize dietary sodium (and water) intake is reaffirmed.

- Not enough evidence to raise minimum of 3 hours of hemodialysis delivered 3 days per week.
  -3 hours 3 days per week is a bare minimum if no residual function.
  -Exceptions……
  ? Patients suffering from poor QOL due to longer treatments
  -Ongoing TiME trial may shed more light on this.
- There is no evidence of harm from extending time.
- Studies advocating limits to ultrafiltration rate are based on observational data only.
- Not enough evidence to make recommendations with regard to dialysate sodium concentration.

Guideline 5. New Hemodialysis Membranes

5.1 We recommend the use of biocompatible high or low flux hemodialysis membranes for intermittent hemodialysis. *(1B)*

Guideline 5. High Flux Membranes

Three large clinical trials:

1. Eknoyan G, Beck GJ, Cheung AK, Daugirdas JT, Greene T, Kusek JW, et al; (**HEMO Study – 1846 pts**). Effect of dialysis dose and membrane flux in maintenance hemodialysis. NEJM 347(25):2010-9, 2002.

2. Locatelli F, Martin-Malo A, Hannedouche T, Loureiro A, Papadimitriou M, Volker Wizemann V, et al. Effect of Membrane Permeability on Survival of Hemodialysis Patients (**MPO Study – 738 pts**). JASN 20:645–654, 2009.

3. Asci G et al., The Impact of Membrane Permeability and Dialysate Purity on Cardiovascular Outcomes (**EGE Study – 704 pts**). JASN 24:1014-1023, 2013.

One meta-analysis:

Palmer SC, Rabindranath KS, Craig JC, Roderick PJ, Locatelli F, Strippoli GF. High-flux versus low-flux membranes for end-stage kidney disease. Cochrane Database Syst Rev. 2012.

Guideline 5. High Flux Membranes

- Three large randomized trials failed to show a survival benefit with high-flux membranes.
- One secondary outcome analysis (HEMO) and a meta-analysis showed reduced cardiovascular mortality with high vs. low-flux.
- Some showed reduced all-cause mortality in certain subgroups:

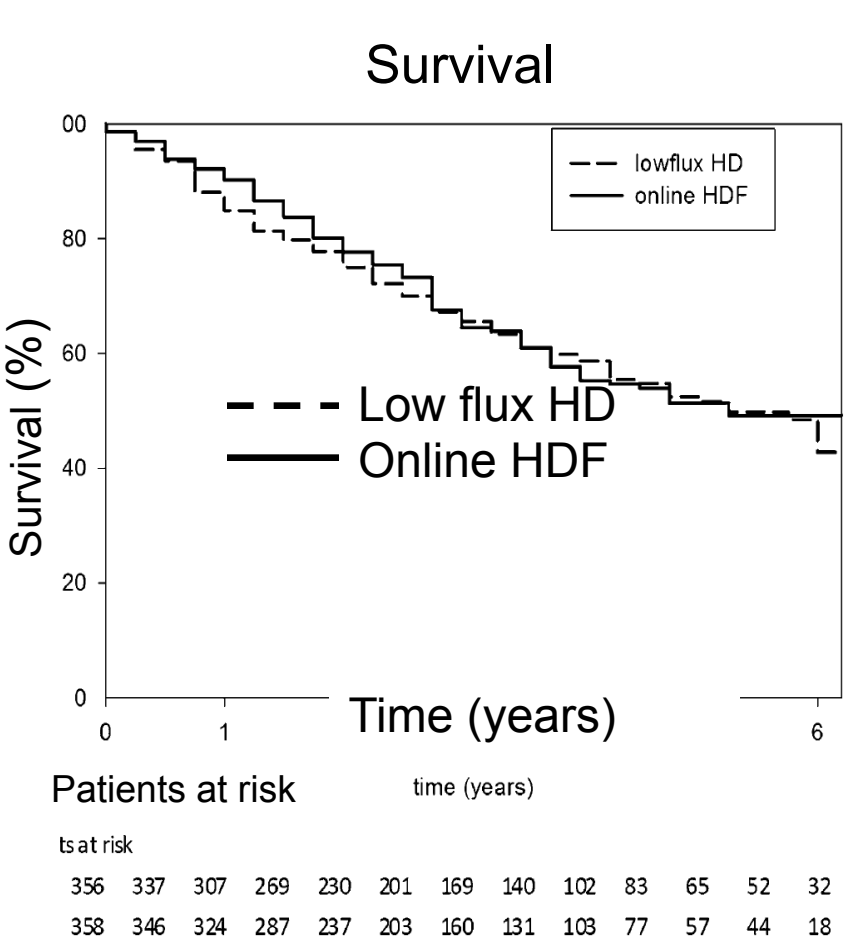
  Low serum albumin (<4 g/dL) [MPO]
  High vintage (> 3.7 years on dialysis) [HEMO]
  Diabetes mellitus [MPO, EGE]
  AV fistulas [EGE]

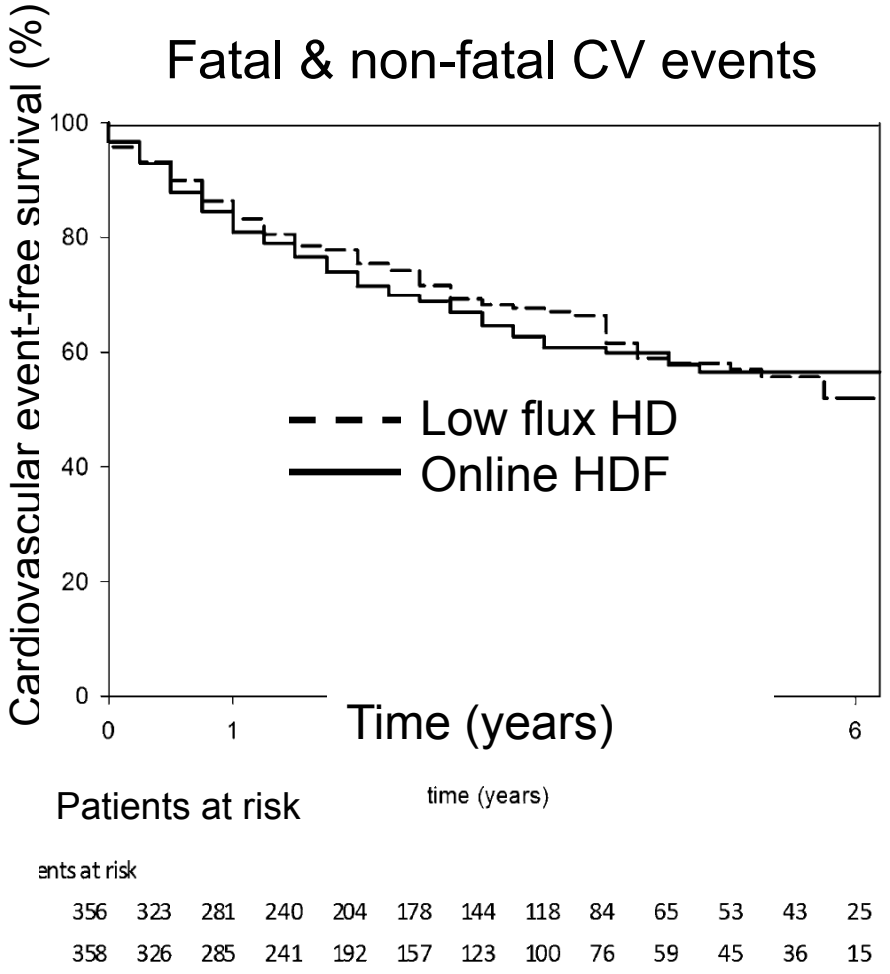
- None showed harm.
- **Because cost of high-flux membranes without strong evidence of benefit, decision to use high vs. low-flux membranes is left up to the treating center.**

Convective Therapies – not recommended at this time

Hemodiafiltration versus Low-Flux Hemodialysis

Grooteman, et al., CONTRAST Study, JASN 2012





2006 and 2015: What's different?

- GRADE: level of recommend (1 & 2) and grade (A-D) of the evidence
- Individualized prescriptions: include patient expectations and preferences
- More prescription flexibility: initiation, frequency, duration, Qf rate
- Less emphasis on absolute minimum or maximum cut-offs
- Recommendations regarding high frequency hemodialysis:
  - No compelling evidence that frequent dialysis is best for everyone
  - Consider for patients with special needs:
    - Left ventricular hypertrophy and/or congestive heart failure
    - Uncontrolled hypertension, fluid overload
    - Metabolic derangements (hyperphosphatemia, hyperkalemia)
    - Sleep apnea
    - Pregnancy (strong recommendation)
  - Acknowledges the risks of frequent hemodialysis
- Consider stdKt/V to measure frequent HD; adjust for Kru, Qf, BSA
- More emphasis on volume and BP control

KDOQI Leadership

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