National Kidney Foundation®

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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## Disclosure Statement

Dr. Suri holds an unrestricted Extramural Research Grant from Baxter Inc.


## Acknowledgement

This slide deck was primarily the effort of Dr. Thomas Depner, KDOQI Hemodialysis Adequacy Co-Chair.

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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.

# Strength of the Recommendation

| | |
|---|---|
| **Level 1**<br>**“We recommend”** | Most patients should receive the recommended course of action. |
| **Level 2**<br>**“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 Categories: HD Update 2015

1. Timing of Hemodialysis Initiation
2. Frequent and Long Duration Hemodialysis
3. Measurement of Dialysis: Urea Kinetics
4. Volume and Blood Pressure Control
5. New Hemodialysis Membranes

# 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)**

# Guideline 1. Timing of Hemodialysis Initiation

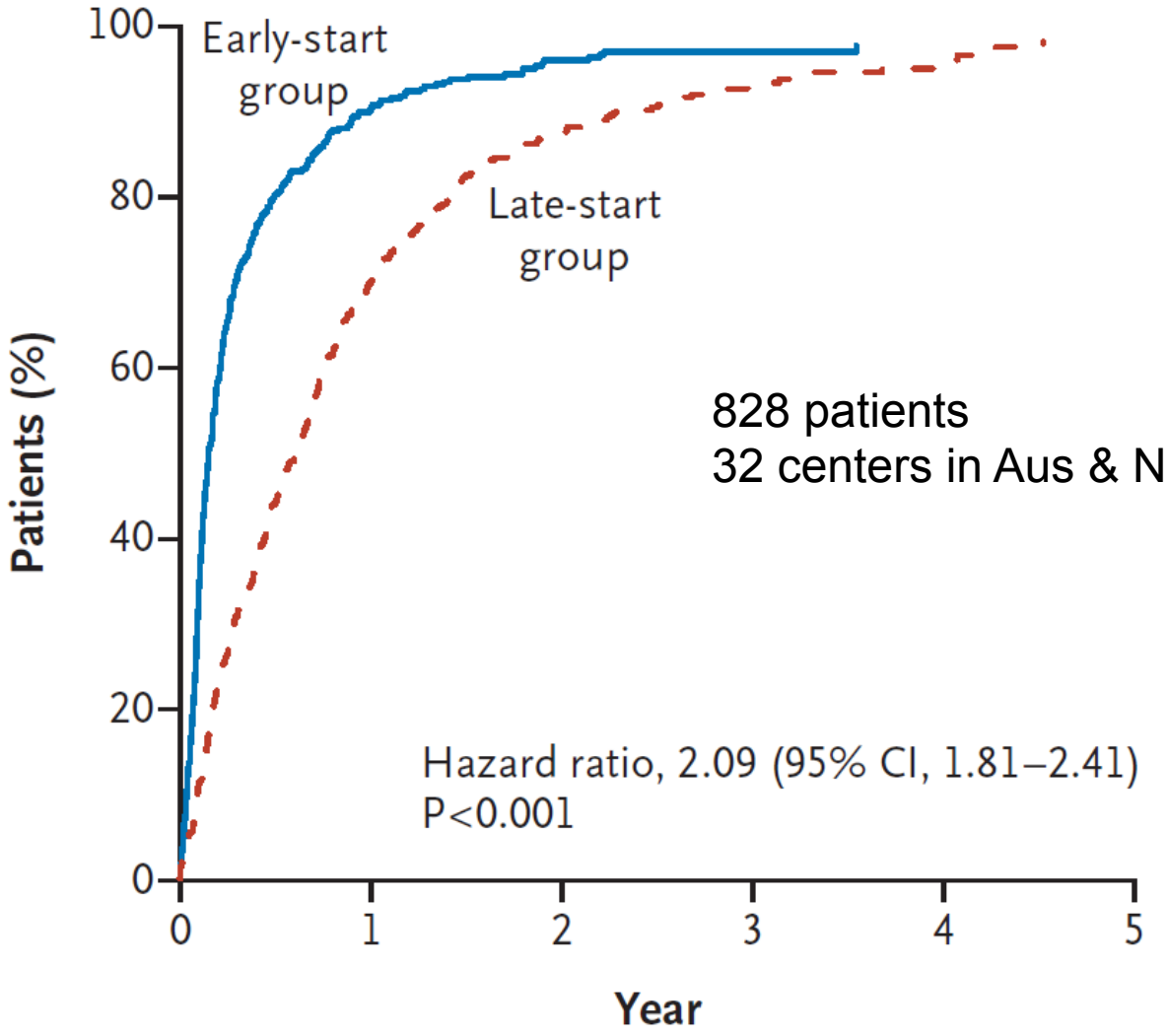
**1.2 The decision to initiate maintenance dialysis in patients who choose to do so should be based primarily upon an assessment of signs and/or symptoms associated with uremia, evidence of protein-energy wasting, and the ability to safely manage metabolic abnormalities and/or volume overload with medical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

# IDEAL Study

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

- 828 patients with CrCl between 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).
- 34% of IDEAL patients had diabetes as cause of ESKD.
- 42% (355/828) had diabetes; randomization was stratified on presence of diabetes
- No difference in time to death, CV or infectious events, or complications of dialysis, cost, cardiac structure or fxn.

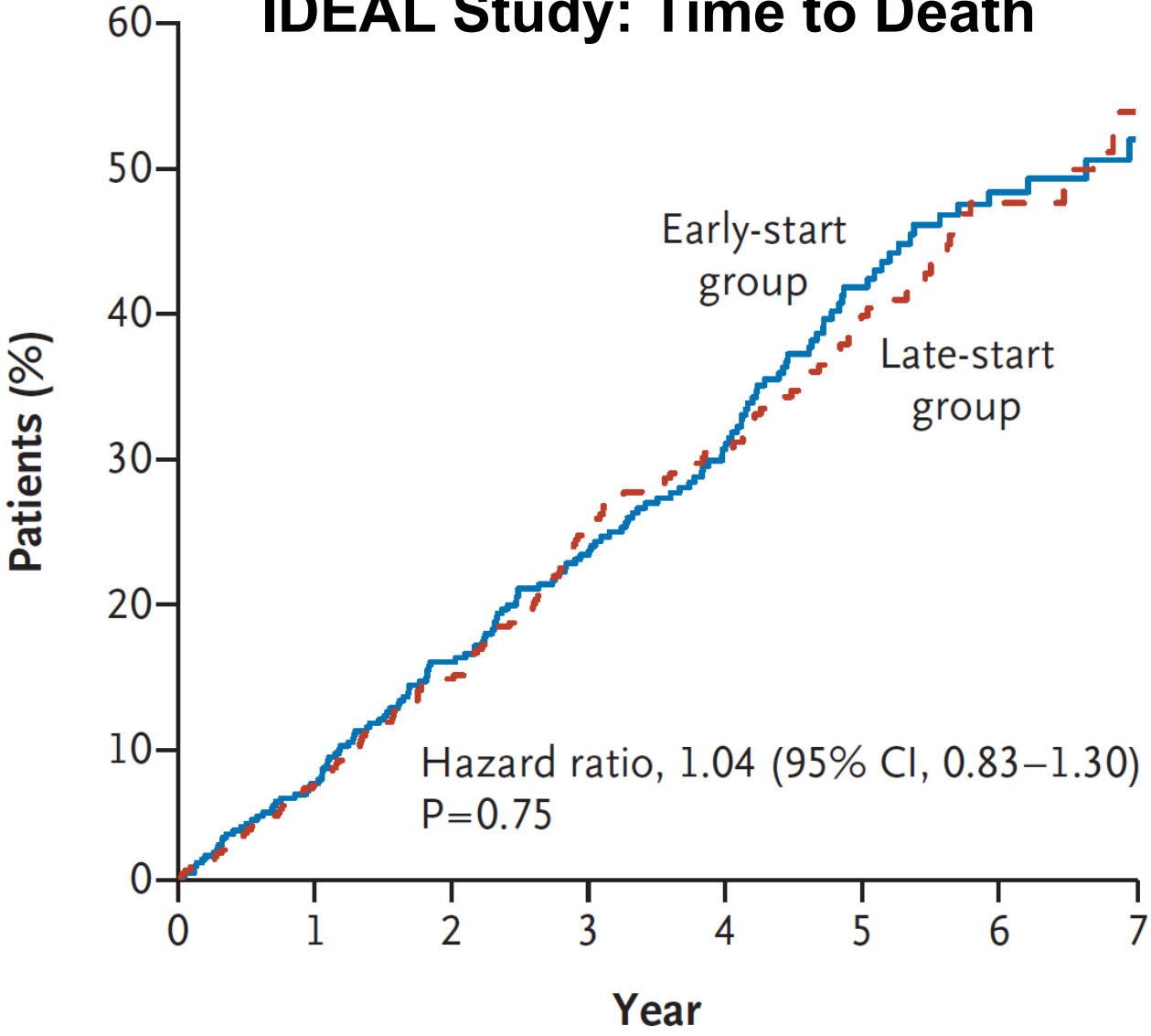
# IDEAL Study: Time to Start of Dialysis




**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 |

# IDEAL Study, subgroup analysis

Subgroup analysis showed no survival benefit of early versus late initiation of hemodialysis (p values 0.26 to 0.74).

- Age
- Sex
- Diabetes
- Body mass index
- History of cardiovascular disease
- Serum albumin level

# IDEAL STUDY: Mortality: Early vs. late start (by subgroup)

| Subgroup | Early Start | Late Start | P Value for Interaction |
|---|---|---|---|
| | *no. of deaths/no. of patients (%)* | | |
| GFR C–G | | | 0.74 |
| <12.5 ml/min/1.73 $m^2$ | 56/139 (40) | 56/137 (41) | |
| ≥12.5 ml/min/1.73 $m^2$ | 96/265 (36) | 99/287 (34) | |
| GFR MDRD | | | 0.58 |
| <9.5 ml/min/1.73 $m^2$ | 58/195 (30) | 57/203 (28) | |
| ≥9.5 ml/min/1.73 $m^2$ | 94/209 (45) | 98/221 (44) | |
| Age | | | 0.26 |
| <60 yr | 39/180 (22) | 38/194 (20) | |
| ≥60 yr | 113/224 (50) | 117/230 (51) | |
| Sex | | | 0.28 |
| Female | 55/143 (38) | 58/143 (41) | |
| Male | 97/261 (37) | 97/281 (35) | |
| Diabetes | | | 0.63 |
| No | 65/232 (28) | 63/241 (26) | |
| Yes | 87/172 (51) | 92/183 (50) | |
| Body-mass index | | | 0.59 |
| <25.0 | 40/102 (39) | 46/126 (37) | |
| 25.0–29.9 | 53/143 (37) | 52/146 (36) | |
| ≥30.0 | 59/159 (37) | 57/152 (38) | |
| Baseline history of cardiovascular disease | | | 0.47 |
| No | 64/244 (26) | 69/262 (26) | |
| Yes | 88/160 (55) | 86/162 (53) | |
| Albumin | | | 0.67 |
| <35 g/liter | 38/68 (56) | 44/81 (54) | |
| ≥35 g/liter | 110/325 (34) | 109/336 (32) | |

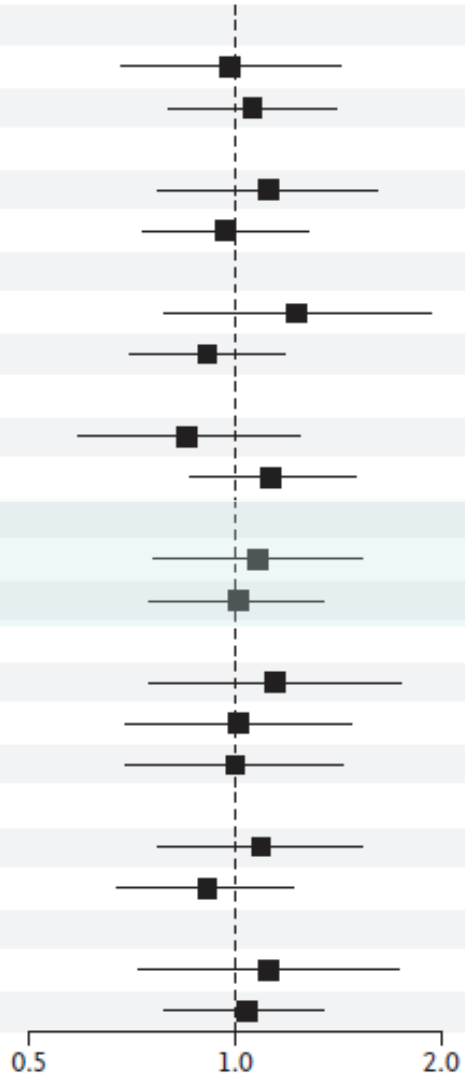



**Figure 3. Effect of the Timing of Dialysis Initiation in Subgroups.** Mortality: Early vs. late start

# IDEAL Study, secondary outcomes

No statistically significant secondary benefits were observed.

- Cardiovascular events
  - Cardiovascular death
  - Nonfatal MI
  - Nonfatal stroke
  - Transient ischemic attack
  - New-onset angina
- Infection events
- Complications of dialysis
- Economic evaluation
- Nutritional status
- Echocardiographic findings
- Quality of life

# 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**

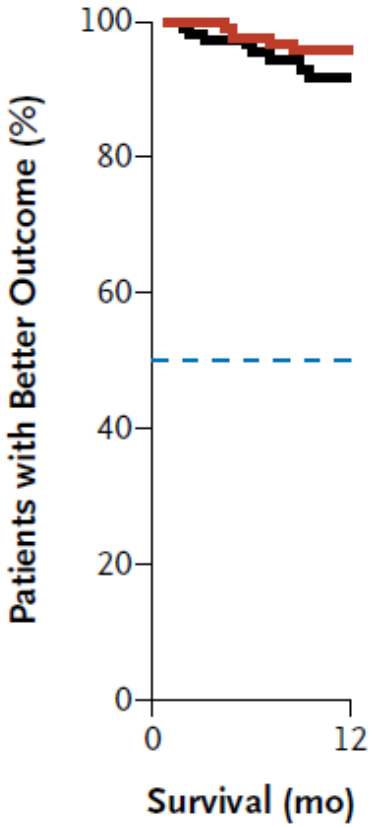
**2.3 Consider home long hemodialysis (6-8 hours, 3 to 6 nights per week) for patients with end-stage kidney disease who prefer this therapy for lifestyle considerations. (ungraded)**

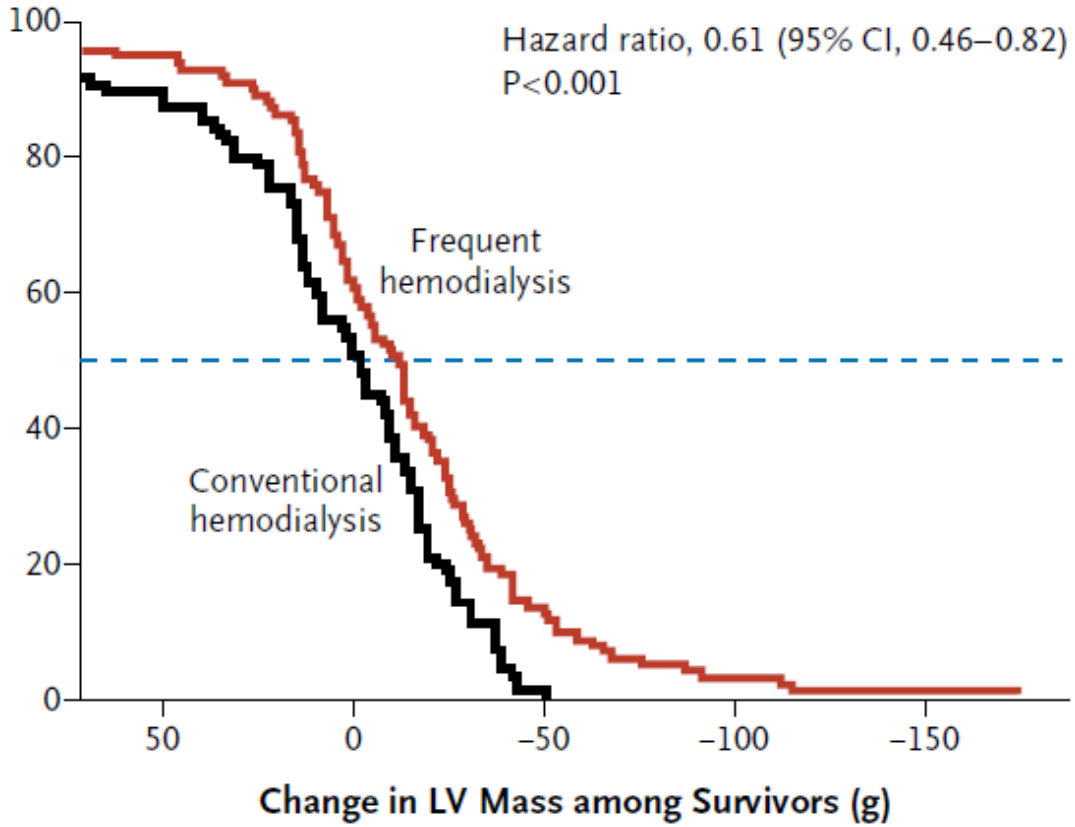
**2.4 We recommend that patients considering frequently administered home long hemodialysis be informed about the risks of this therapy, including possible increase in vascular access complications, potential for increased caregiver burden, and possible accelerated decline in residual kidney function.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

# FHN short daily in-center hemodialysis

Primary outcomes

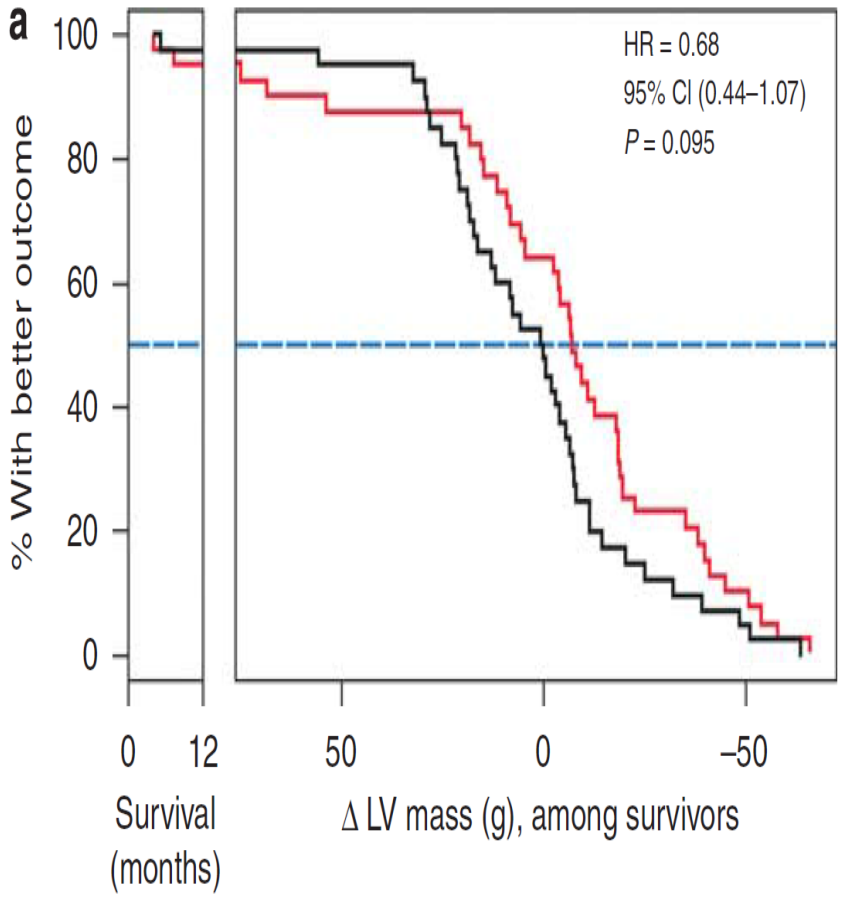



Chertow, et al., NEJM 2010

# FHN nocturnal home hemodialysis

## Primary outcomes

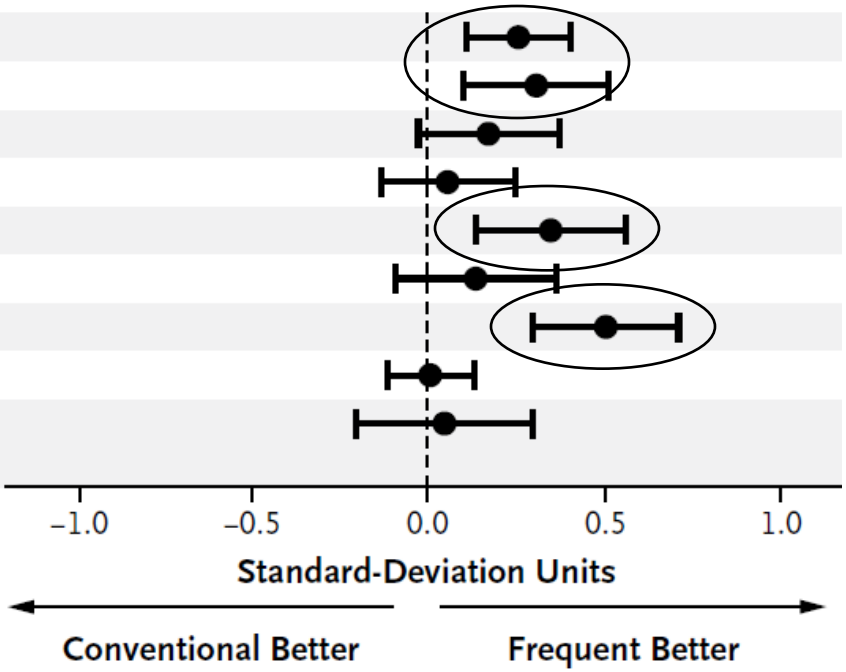



Rocco, et al., KI 2012

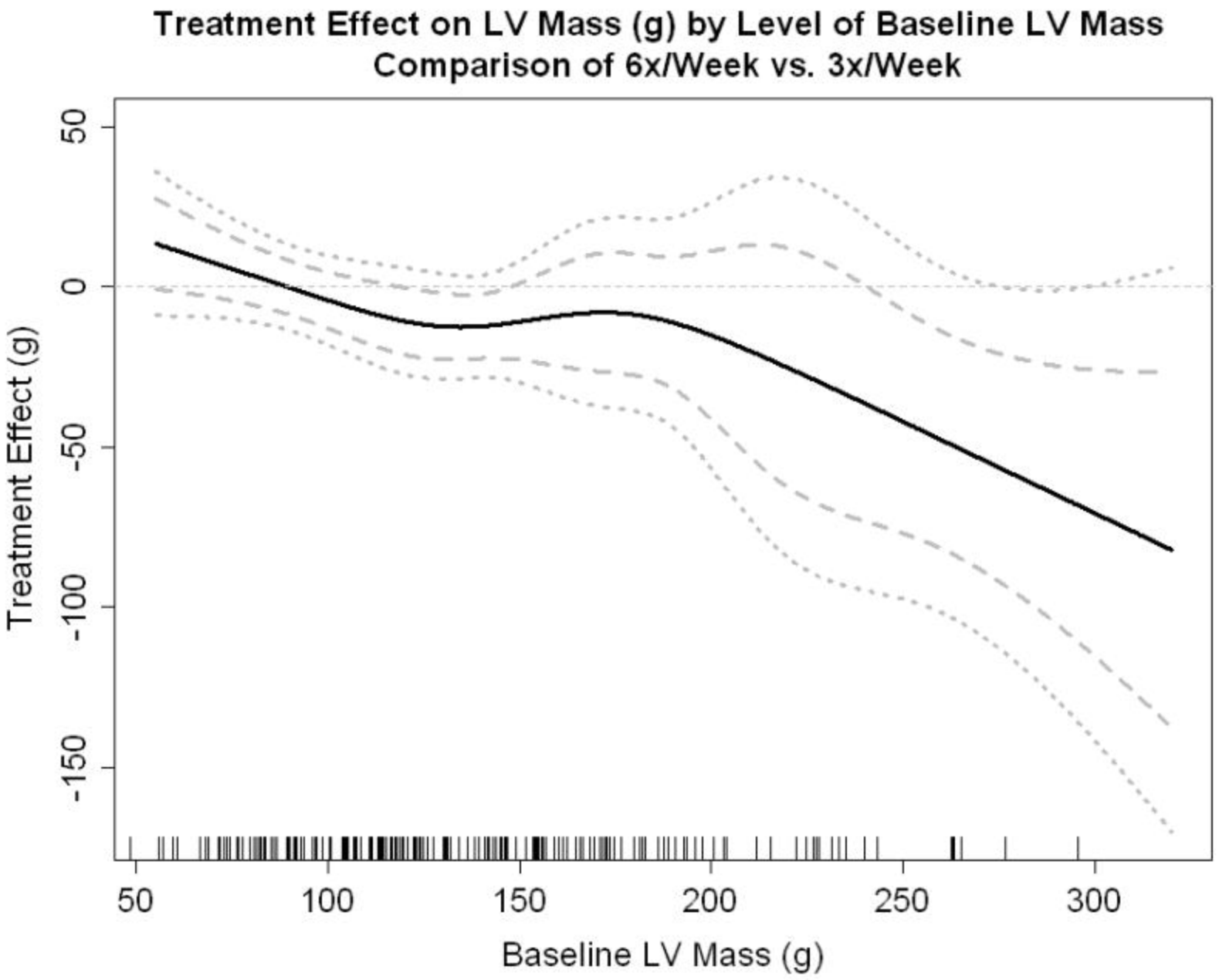
# FHN short daily in-center hemodialysis

## 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 |




Chertow, et al., NEJM 2010




Chan CT et al. Circ Cardiovas Imaging 2012

# Frequent dialysis ("short daily") in patients with substantial Kru

- No trend for a benefit on LVH or LVED when Kru > 100 ml/day (FHN)

| | | ΔLV mass | P value |
|---|---|---|---|
| Baseline urine volume | ≤100 mL | −17.4 (−27.2 to −7.5) | 0.15 |
| | >100 mL | −3.6 (−18.3 to 11.2) | |

# Long frequent versus standard dialysis during pregnancy: Canadian Study

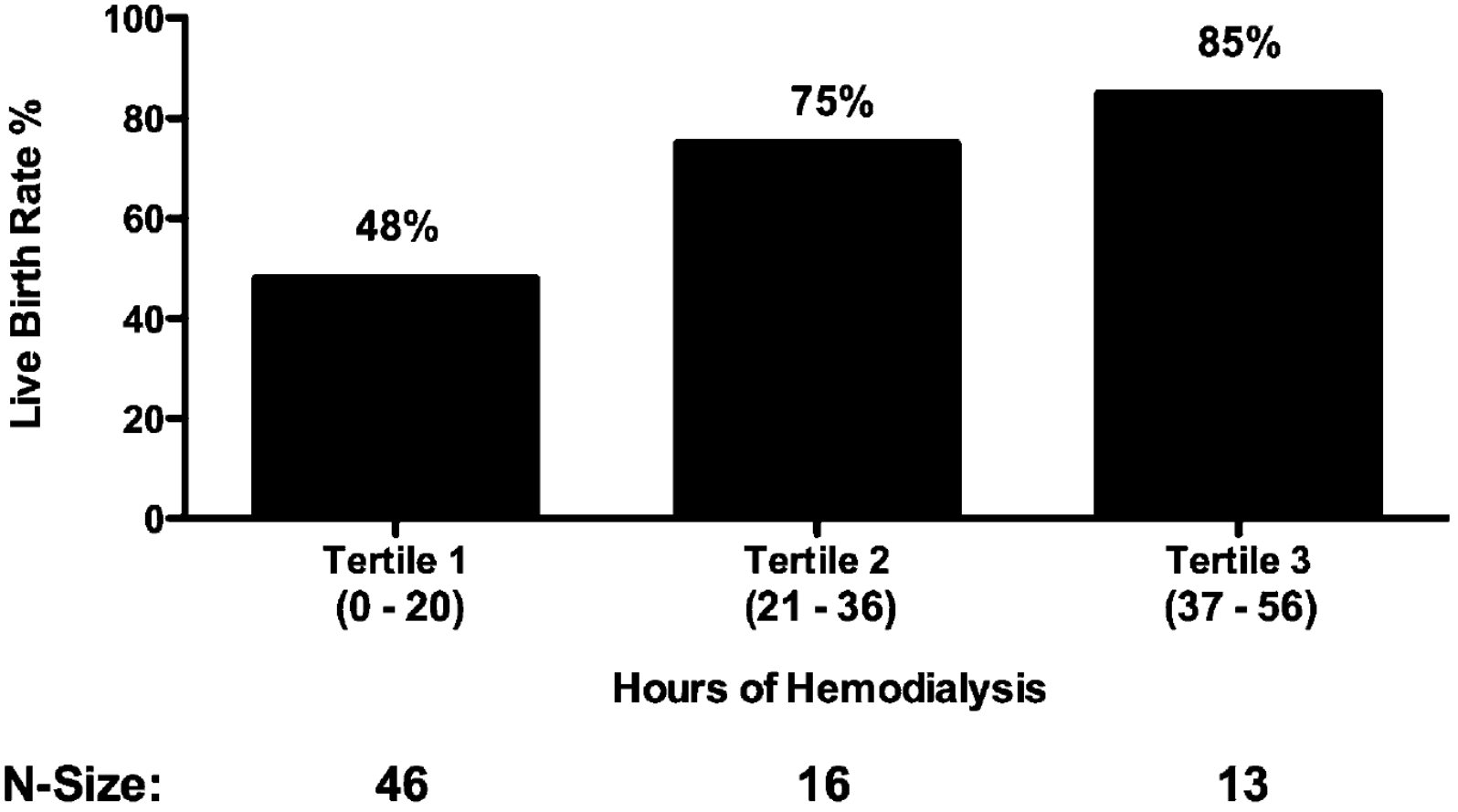
| Source | N | Td (hrs) | Pd (wks) | birth rate | birth wt (gms) |
|---|---|---|---|---|---|
| Canadian | 22 | 43 ± 6 | 36 | 86.4% | 2118 ± 857 |
| US Registry | 70 | 17 ± 5 | 27 | 61.4% | 1748 ± 949 |

Td: hours of dialysis/week
Pd: duration of pregnancy in weeks

Hladunewich MA, et al: Intensive hemodialysis associates with improved pregnancy outcomes: a Canadian and United States cohort comparison. JASN 25(5):1103-9, 2014

# Pregnancy and dialysis: Canadian birth rate correlates with dialysis intensity

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



# Guideline 3. Measurement of HD: Urea Kinetics

**3.1** We recommend a target single pool Kt/V (spKt/V) of 1.4 per hemodialysis session for patient 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)

# Guideline 3. Measurement of HD: Urea Kinetics

- Small solute clearance is the primary goal of dialysis without which anuric survival is impossible.
- Control of volume and urea concentrations in the patient are not the primary goals of dialysis.
- $Kt/V_{urea}$ is an easily obtained measure of small solute clearance per treatment, normalized to body size.
- As expected, $Kt/V_{urea}$ predicts morbidity and mortality in controlled clinical trials.
- Treatment of the patient should not stop after achieving an "adequate" $Kt/V_{urea}$.

# How to calculate standard Kt/V

$$eKt/V = spKt/V\ (t/(t + 30))$$ (Tattersall)

$$stdKt/V = \frac{10080\,\frac{1 - e^{-eKt/V}}{t}}{\frac{1 - e^{-eKt/V}}{eKt/V} + \frac{10080}{Nt} - 1}$$ (Gotch, Leypoldt)

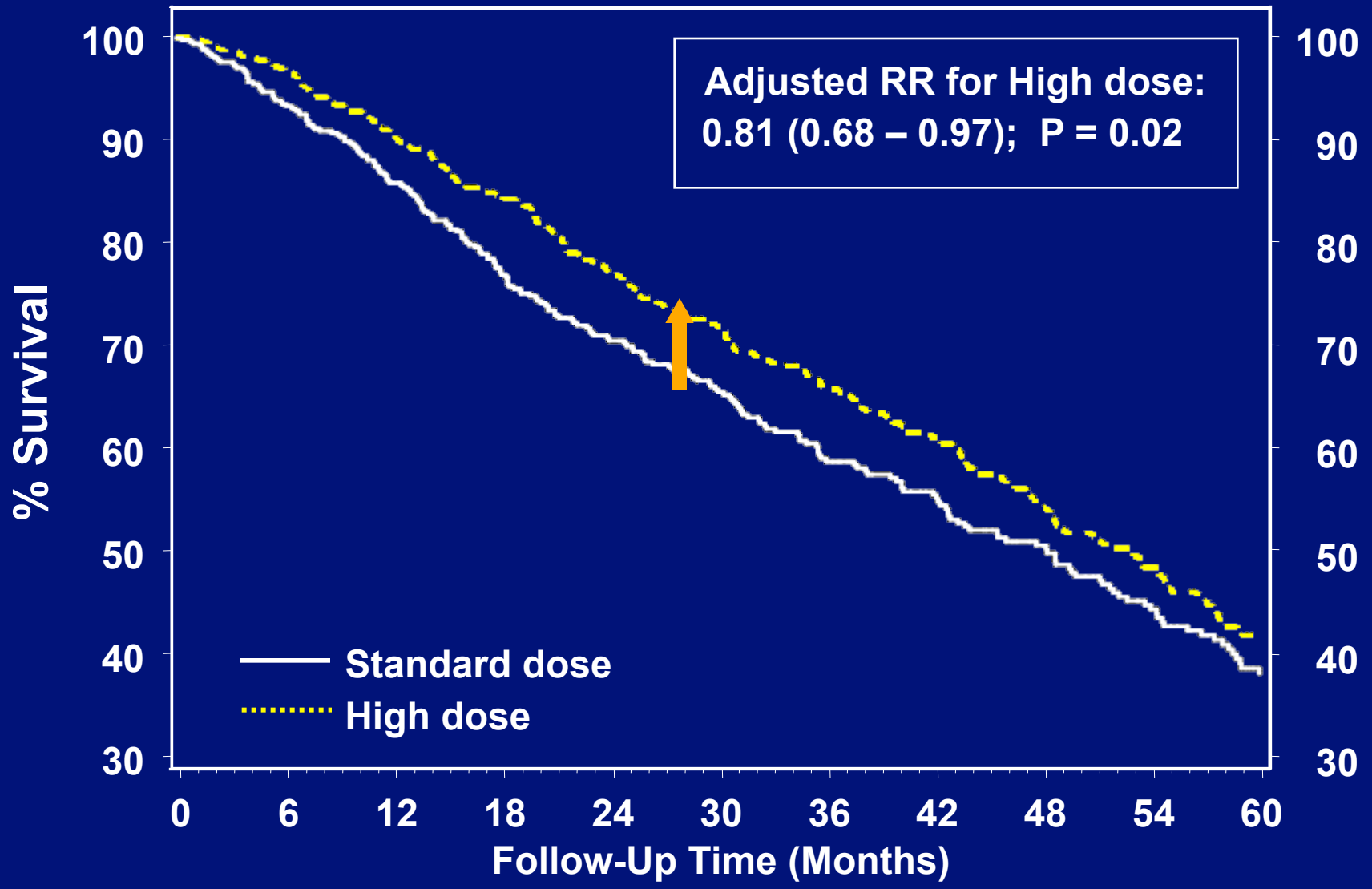
$$stdKt/V = \frac{S}{1 - \frac{0.74}{F}\left[\frac{U_f}{V}\right]} + K_r\frac{10080}{V}$$ (Daugirdas)

# Surface area normalized $_{std}$Kt/V

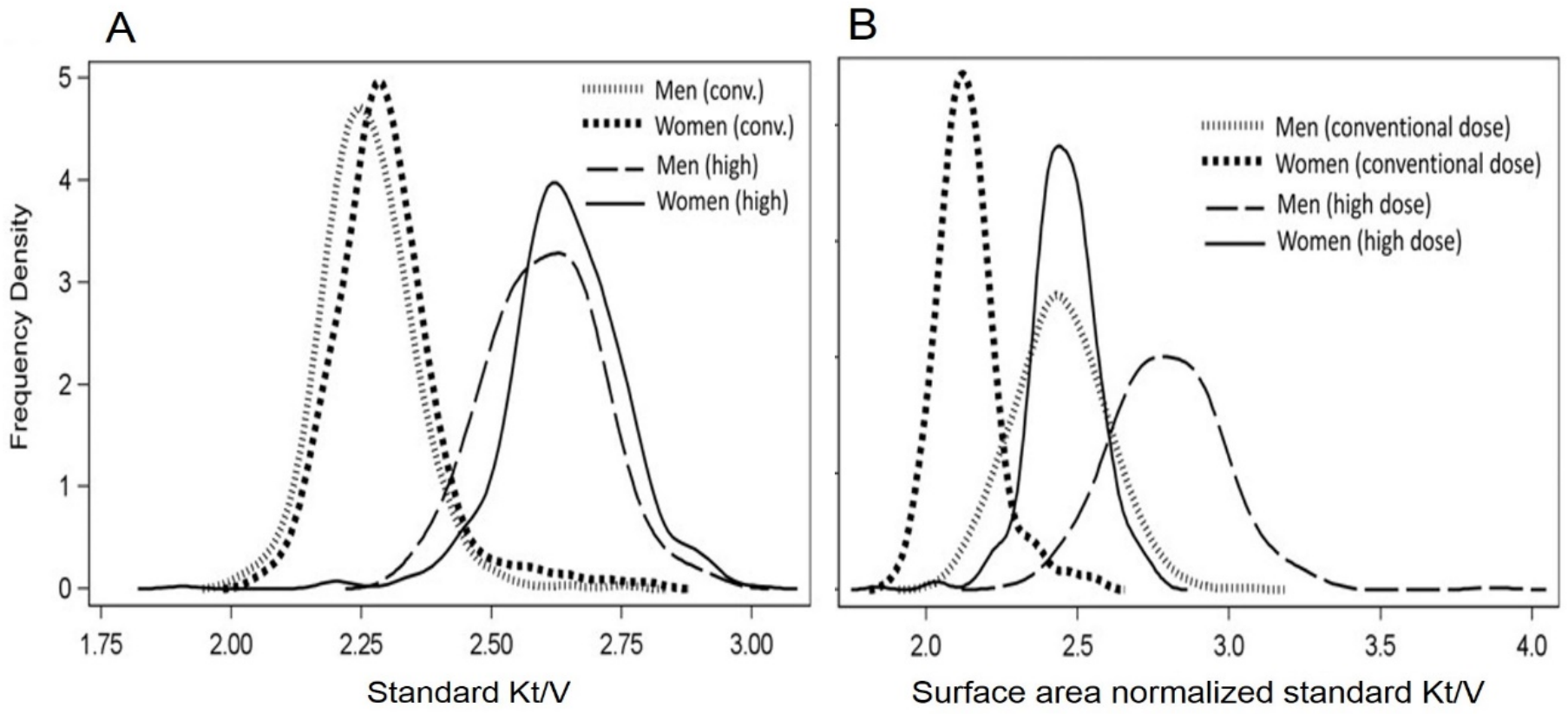
$$SA_{stdKt/V} = \frac{{}_{std}Kt/V}{20} \bullet \frac{V_W}{BSA}$$

Vw is Watson estimate of total body water
BSA is body surface area

# Time to Death by Dose
## Women (484 Deaths)



# Effect of Surface Area Normalization




Daugirdas, et al, CJASN 2010

Guideline 4.

# Volume & 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 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 dialysis across the board.**

  **3 hours is a bare minimum.**

  **Exceptions……**

  **Ongoing TiME trial may shed more light on this.**

- **No evidence of harm from extending time.**
- **Studies advocating limits to ultrafiltration rate are based on observational data only.**
- **No recommendation 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:

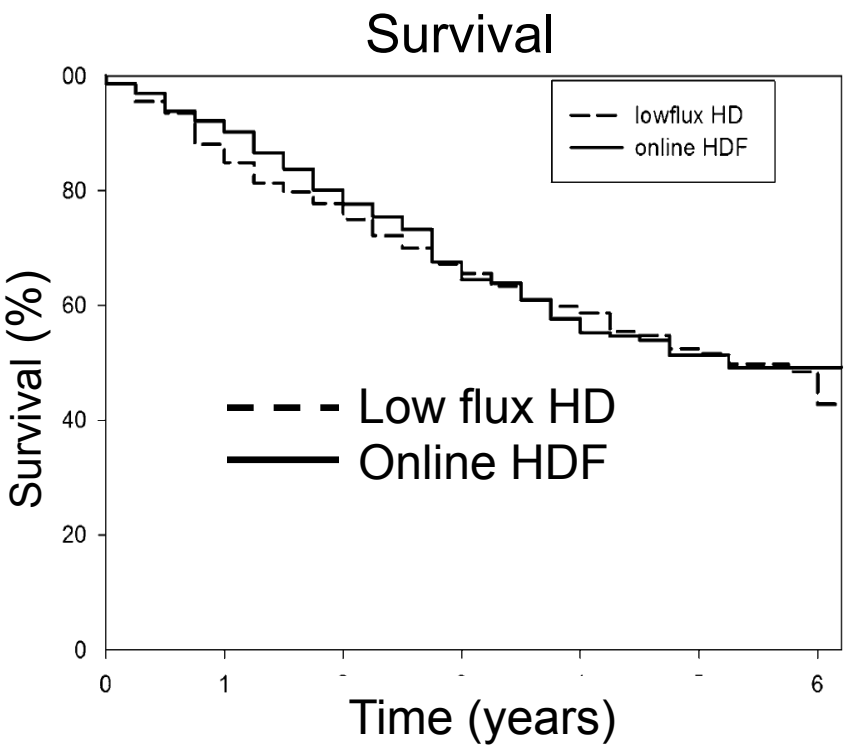
Palmer SC, Rabindranath KS, Craig JC, Roderick PJ, Locatelli F, Strippoli GF. High-flux versus low-flux membranes for end-stage kidney disease. Cochrane Database Syst Rev. 2012.

# Guideline 5. High Flux Membranes

- Three large randomized trials failed to show a survival benefit.
- One secondary outcome analysis (HEMO) and a meta-analysis showed reduced cardiovascular mortality.
- Some showed reduced all-cause mortality in subgroups:
  - For pre-specified subgroups:
    - Low serum albumin (<4 g/dL) [MPO]
    - High vintage (> 3.7 years on dialysis) [HEMO]
  - For post-hoc subgroups:
    - Diabetes mellitus [MPO, EGE]
    - AV fistulas [EGE]
- None showed harm.
- Cost may be a consideration in some venues.

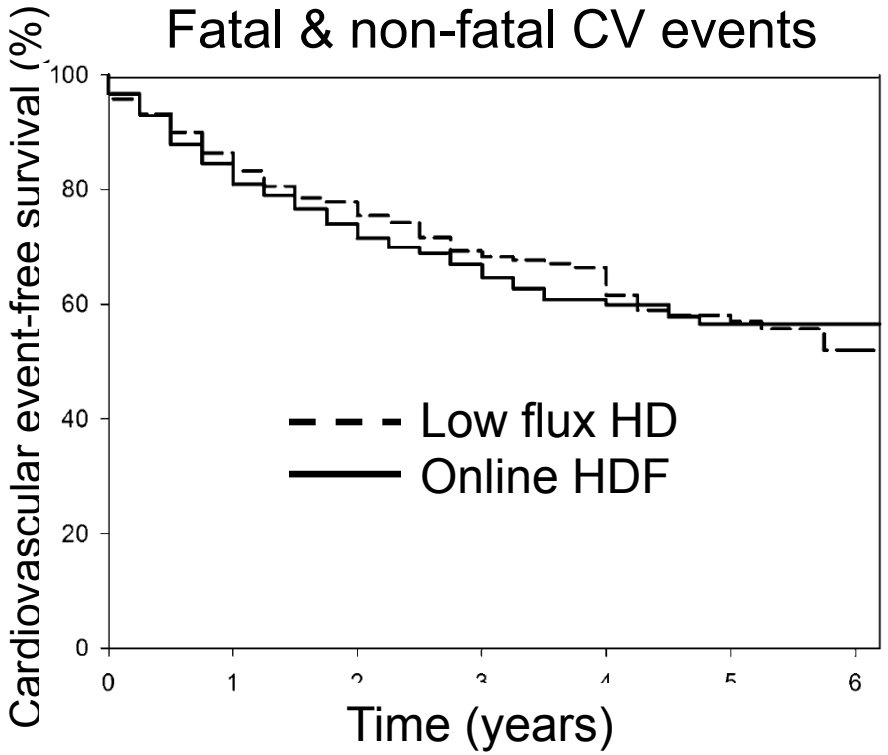
# Hemodiafiltration versus Low-Flux Hemodialysis

Grooteman, et al., CONTRAST Study, JASN 2012




Patients at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 356 | 337 | 307 | 269 | 230 | 201 | 169 | 140 | 102 | 83 | 65 | 52 | 32 |
| 358 | 346 | 324 | 287 | 237 | 203 | 160 | 131 | 103 | 77 | 57 | 44 | 18 |




Patients at risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 356 | 323 | 281 | 240 | 204 | 178 | 144 | 118 | 84 | 65 | 53 | 43 | 25 |
| 358 | 326 | 285 | 241 | 192 | 157 | 123 | 100 | 76 | 59 | 45 | 36 | 15 |

# 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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