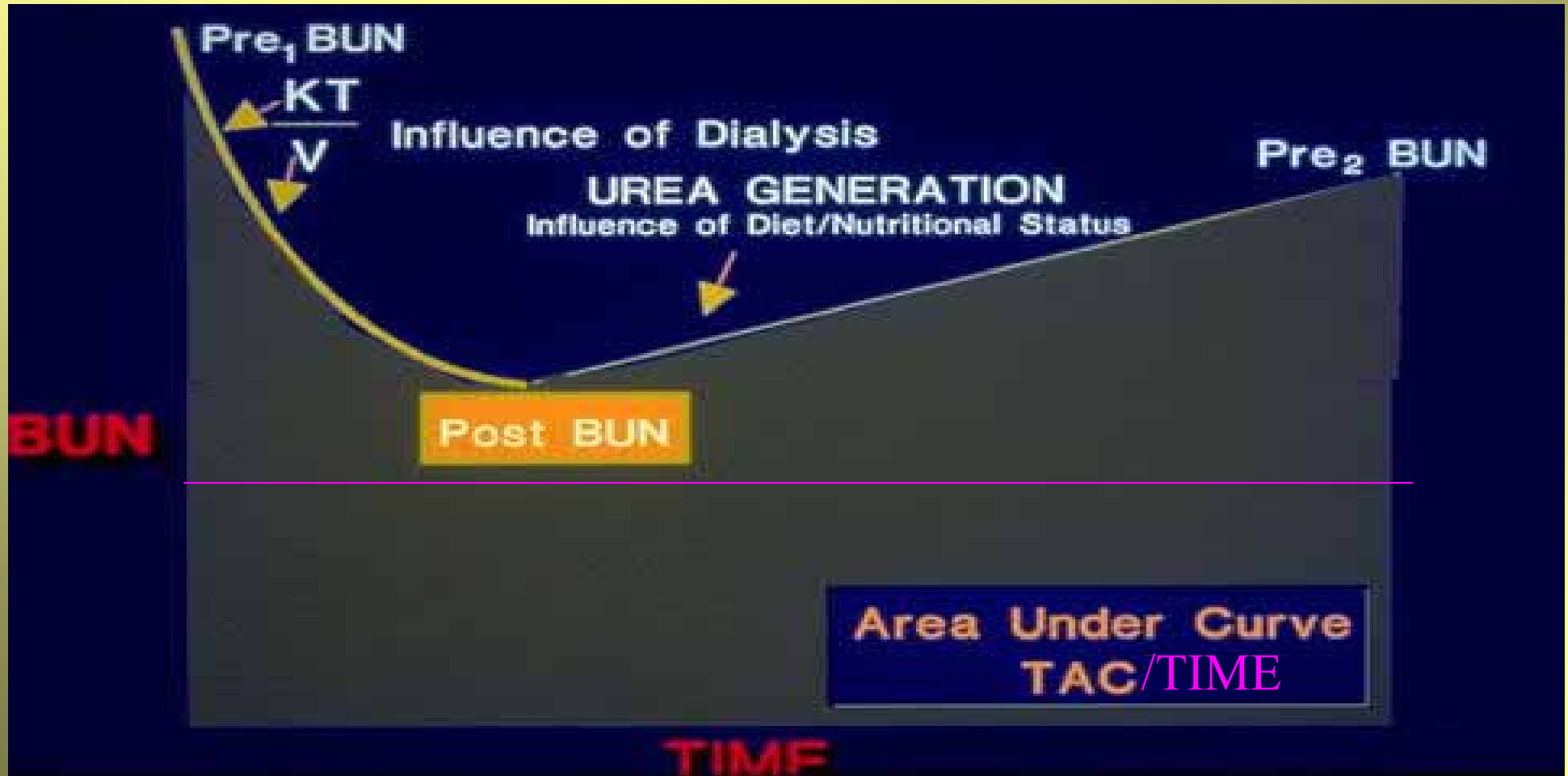


THE HEMODIALYSIS PRESCRIPTION: TREATMENT ADEQUACY

**GERALD SCHULMAN MD
VANDERBILT UNIVERSITY
MEDICAL SCHOOL
NASHVILLE, TENNESSEE**

THE DIALYSIS CYCLE



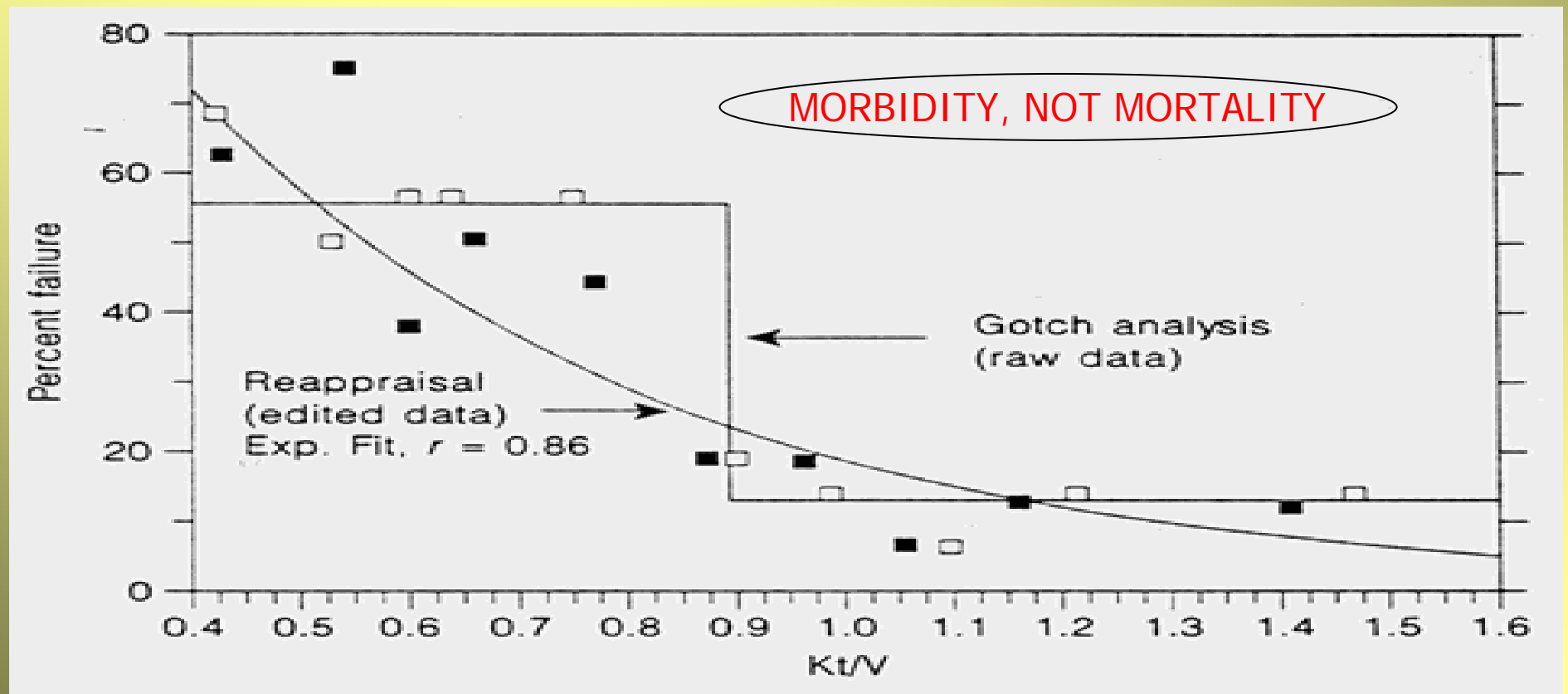
DESIGN OF THE NATIONAL COOPERATIVE DIALYSIS STUDY

TABLE 7 CONTROL ACHIEVED ACCORDING TO STUDY GROUP

Group and Factor Analyzed	Duration of Dialysis (Hr:Min)	Midweek Predialysis BUN (mg/dl) Mean \pm S.E.M.	Time-Averaged BUN (mg/dl) Mean \pm S.E.M.
I	4:29 \pm 0:03	71.2 \pm 1.4	51.3 \pm 1.1
II	4:31 \pm 0:03	104.9 \pm 1.7	87.7 \pm 1.4
III	3:19 \pm 0:03	73.1 \pm 1.4	54.1 \pm 1.1
IV	3:14 \pm 0:03	109.1 \pm 1.5	89.6 \pm 1.2
TIME*	P < 0.0001	P < 0.05	P < 0.05
BUN*	P > 0.1	P < 0.0001	P < 0.0001
Interaction*	P > 0.1	P > 0.1	P > 0.1

* The probabilities indicate the significance of differences between means for the variable with respect to the experimental factor. (Reproduced with permission from Lowrie EG, Laird NM, Parker TF, Sargent JA, *The effect of the hemodialysis prescription on patient morbidity*, *N Engl J Med* 1981; 305:1176-1181.)

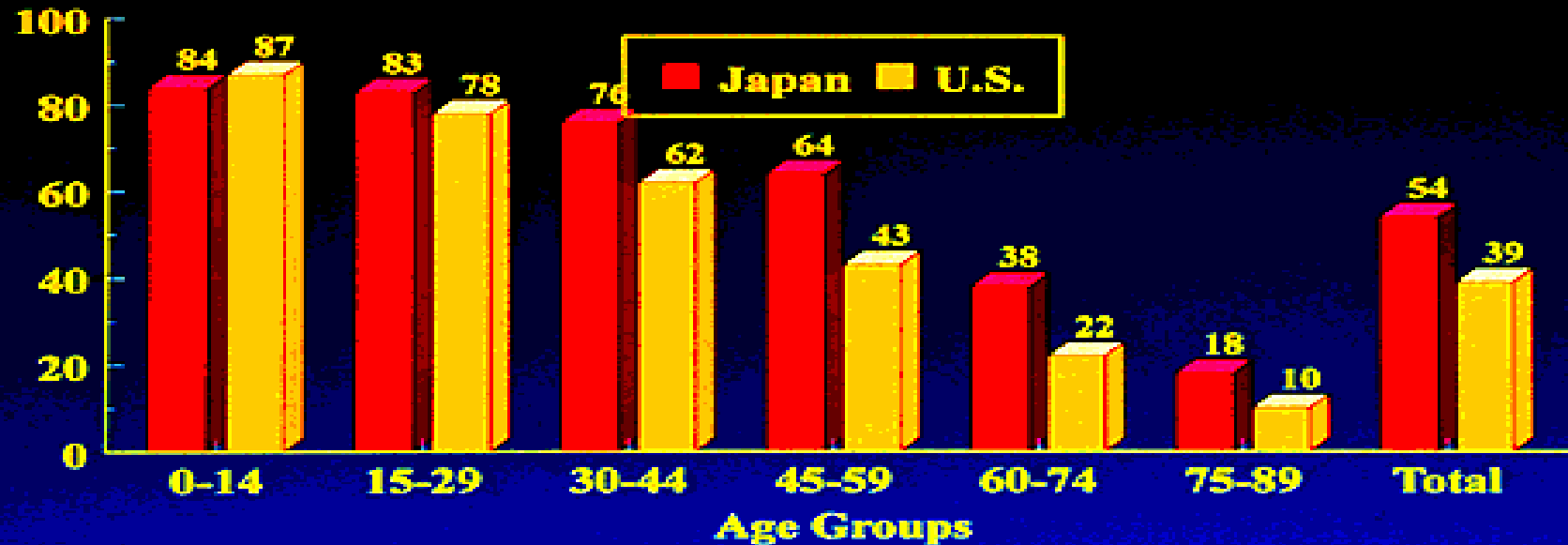
REVISED NCDS RESULTS EXPRESSED AS Kt/V



COMPARATIVE MORTALITY RATES

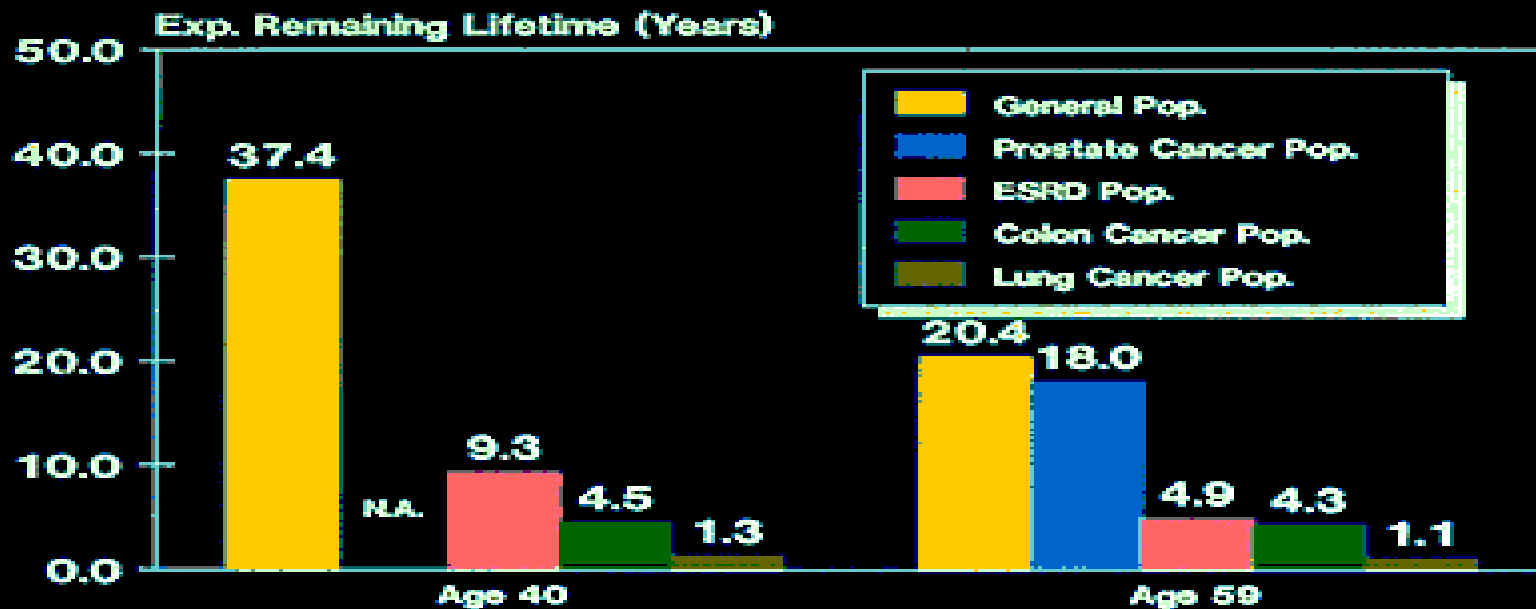
Five year RRT survival for U.S. vs. Japan (by age)

5-Yr. Survival Rate



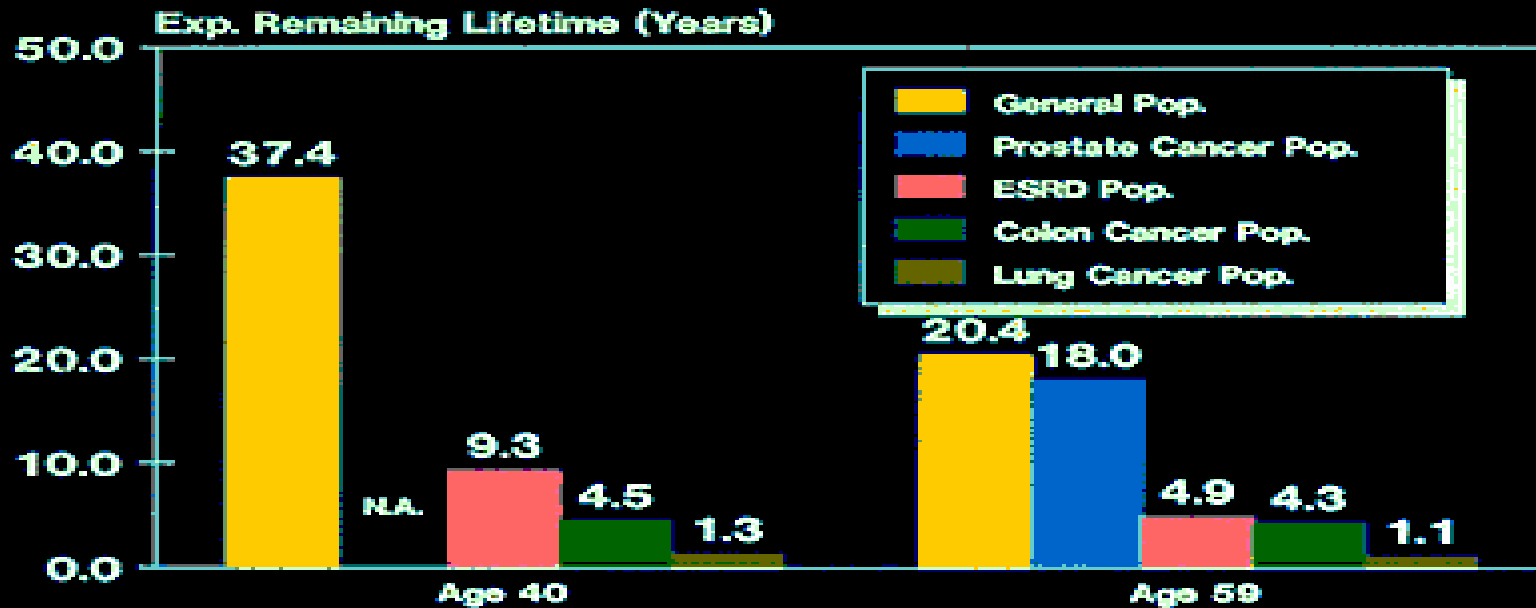
IMPLICATION OF US DIALYSIS MORTALITY RATE

Expected Remaining Lifetime: ESRD, Cancer (3 types) & General Population Age 40 and 59, 1988



IMPLICATION OF US DIALYSIS MORTALITY RATE

Expected Remaining Lifetime: ESRD, Cancer (3 types) & General Population Age 40 and 59, 1988



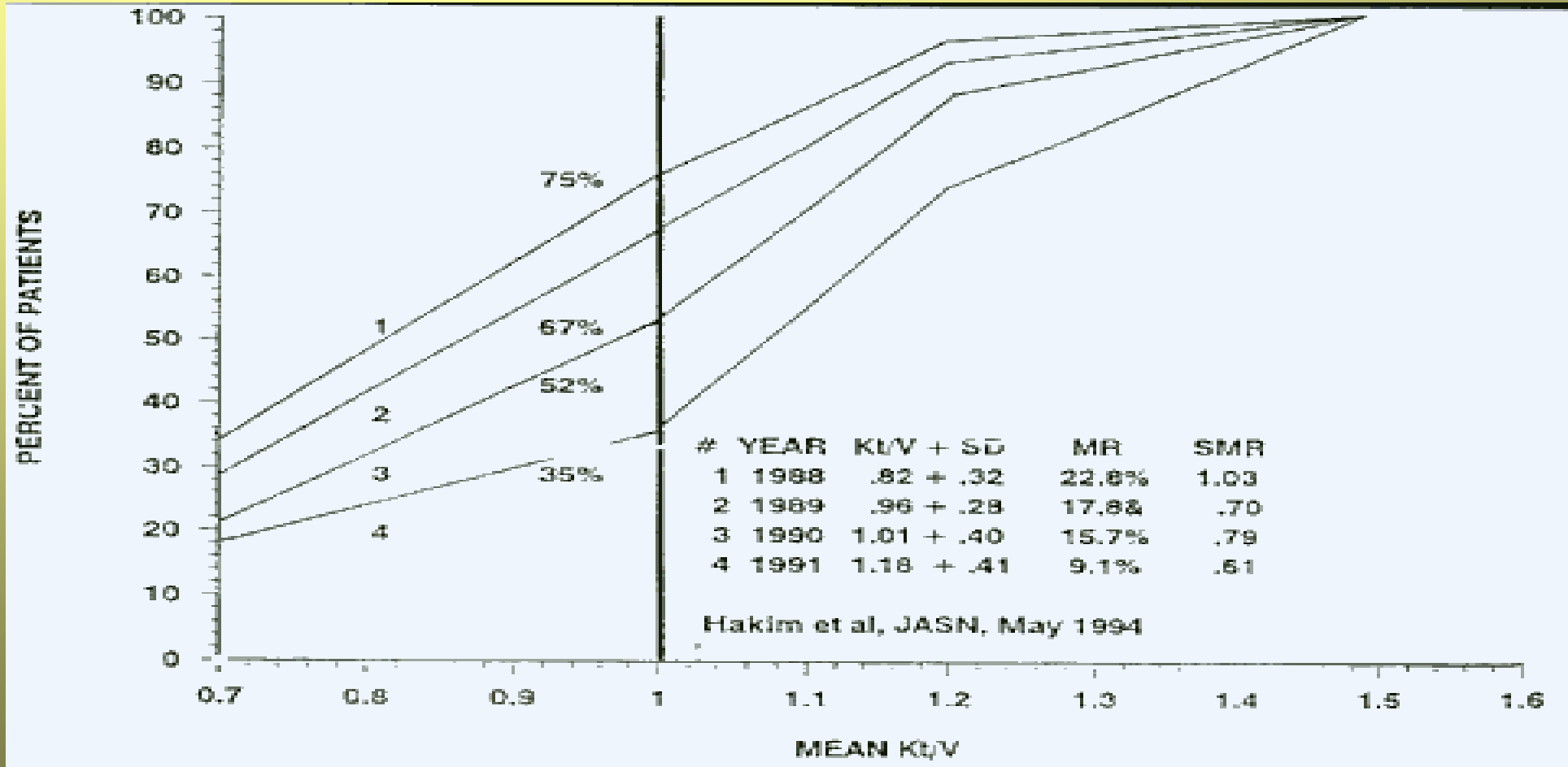
TASSIN EXPERIENCE

Table 6. Survival in a Dialysis Unit With Kt/V of 1.67

Initial Age (yr)	No. of Patients	Survival			
		5-Year	10-Year	15-Year	20-Year
<35	112	93%	88%	80%	71%
35-44	84	92%	81%	63%	39%
45-54	111	88%	76%	53%	—
55-64	98	83%	60%	21%	—
>64	40	69%	64%	—	—
All patients	445	87%	75%	55%	43%

Data from Laurent et al.⁷¹

Kt/V AND MORTALITY



Kt/V & RISK OF MORTALITY

<u>KT/V</u>	<u>RR</u>	
	no DM n = 1082	DM 691
1.0 < 1.2	1.00	1.00
1.2 < 1.4	0.64	0.70
≥ 1.4	0.67	0.60

Kt/V & MORTALITY: MINNESOTA EXPERIENCE

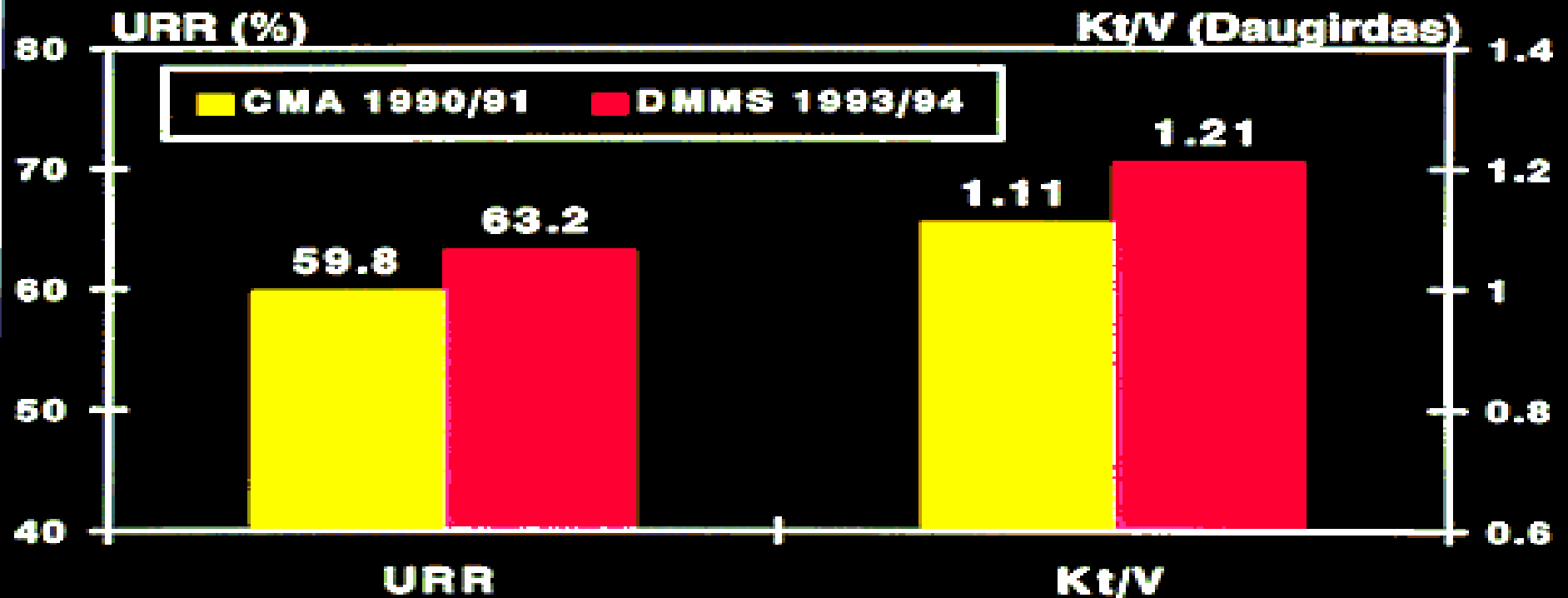
Cox Regression Analysis

	Kt/V	Relative Risk	p Value
Nondiabetic N=1082	↑ 0.1	0.95	0.012
Diabetic N=691	↑ 0.1	0.93	0.004

Adapted from Collins, et al. AJKD 23:272, 1994

CHANGING TRENDS IN THERAPY

Delivered Kt/V and URR for HD Patients* Prevalent > 1 year, 1991 and 1994

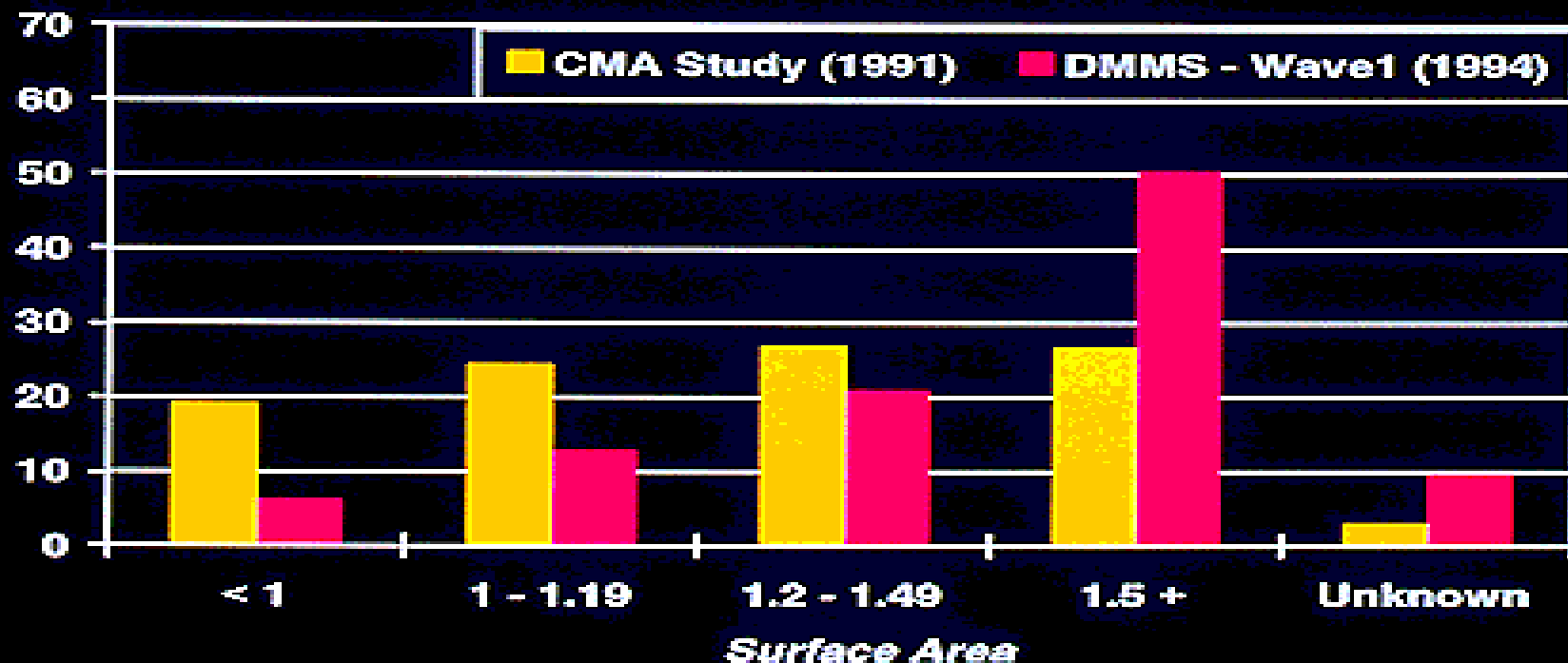


* only for thrice weekly HD

CHANGING TRENDS IN THERAPY

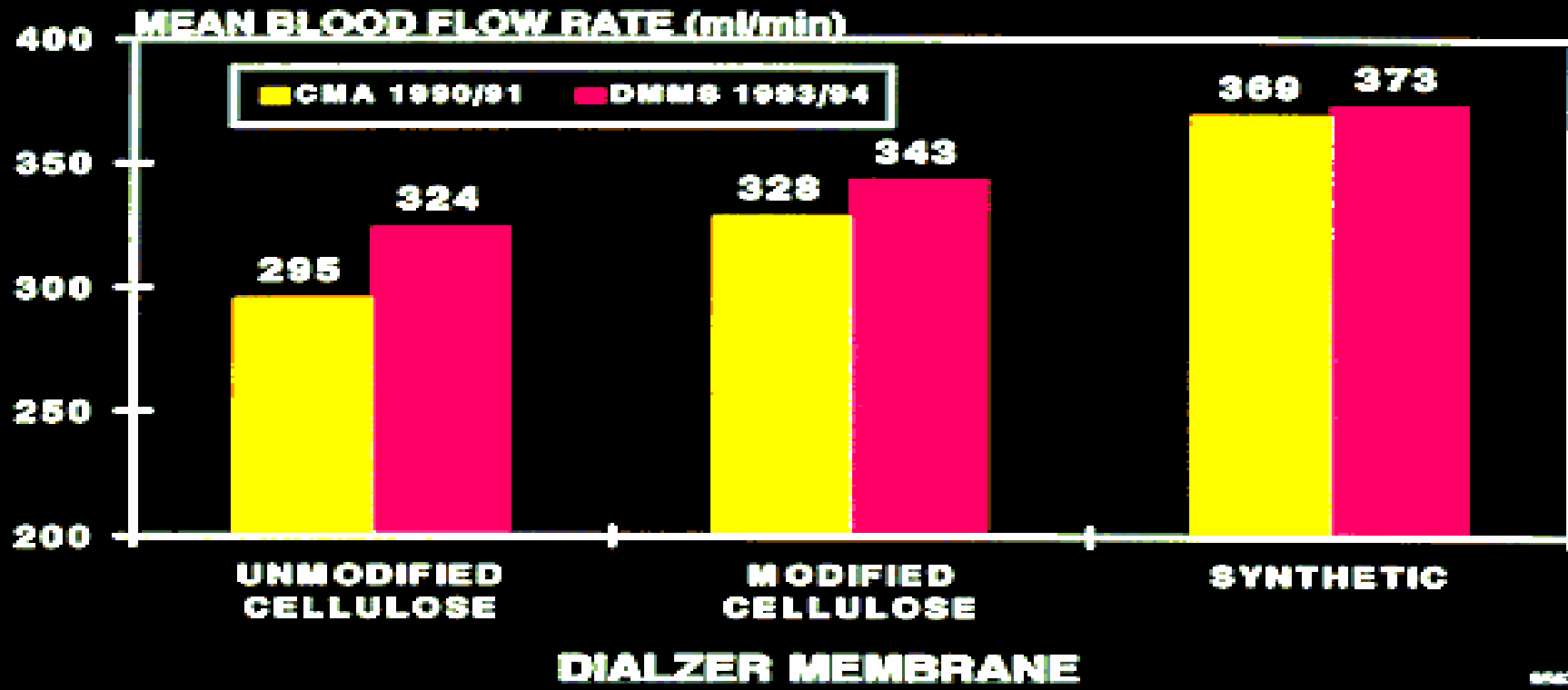
Distribution of Surface Area in Dialyzers Used by Hemodialysis Patients, 1991 and 1994

% of Patients



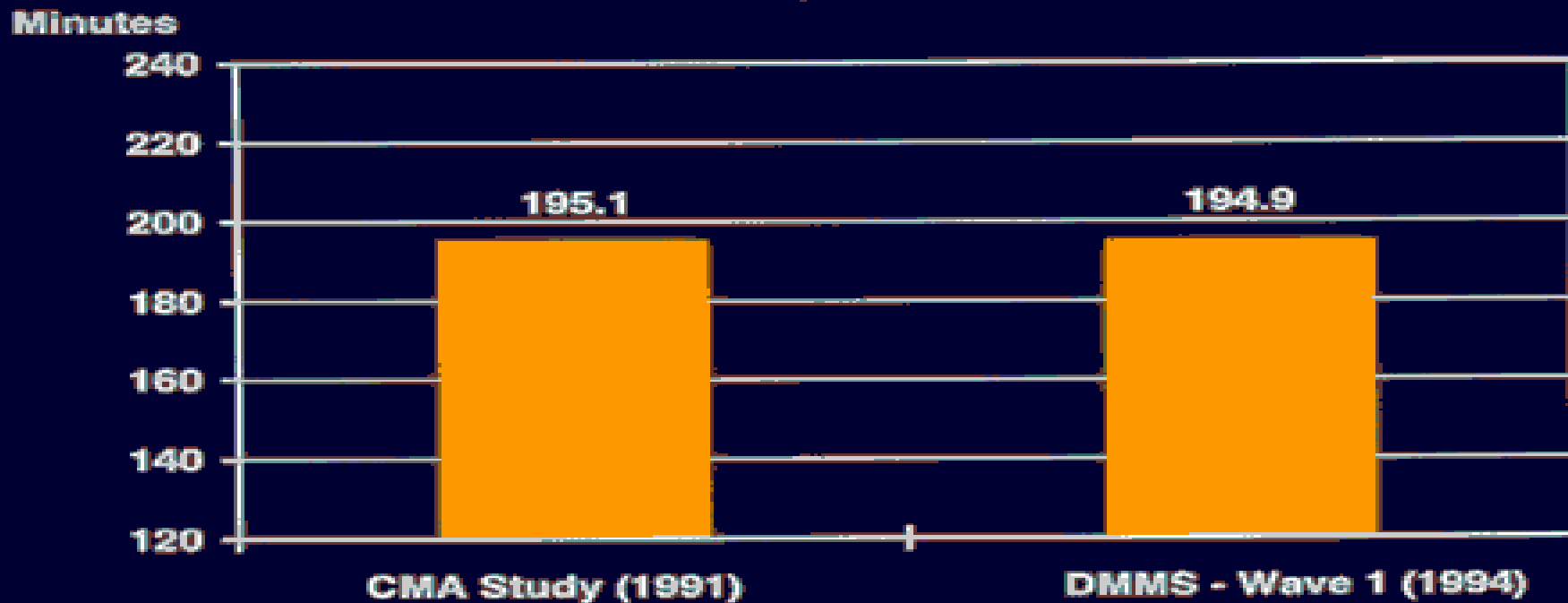
CHANGING TRENDS IN THERAPY

Blood Flow by Membrane, 1991 and 1994



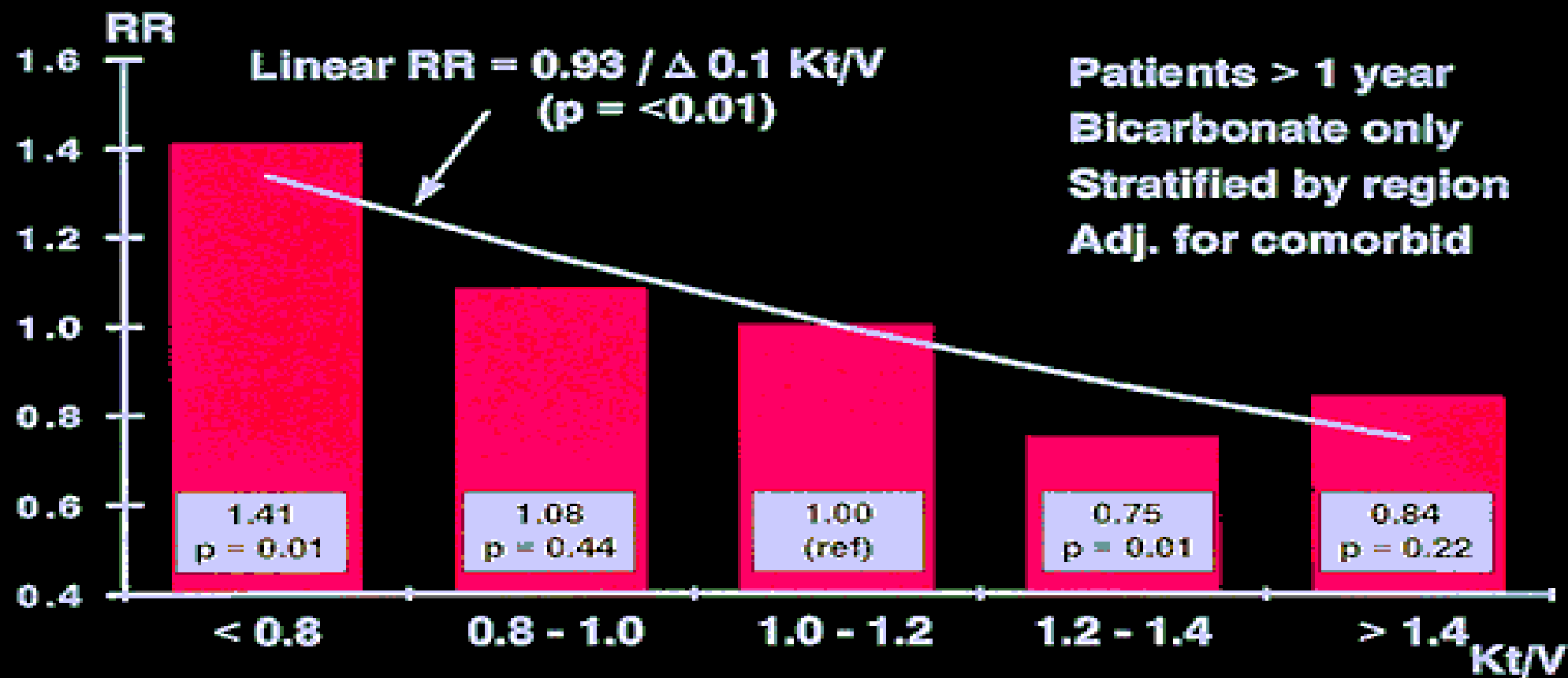
CHANGING TRENDS IN THERAPY

Mean Treatment Time for Hemodialysis Patients*, 1991 and 1994



* Only patients on 3 times/week schedule

Mortality by Delivered Kt/V, 1990-93

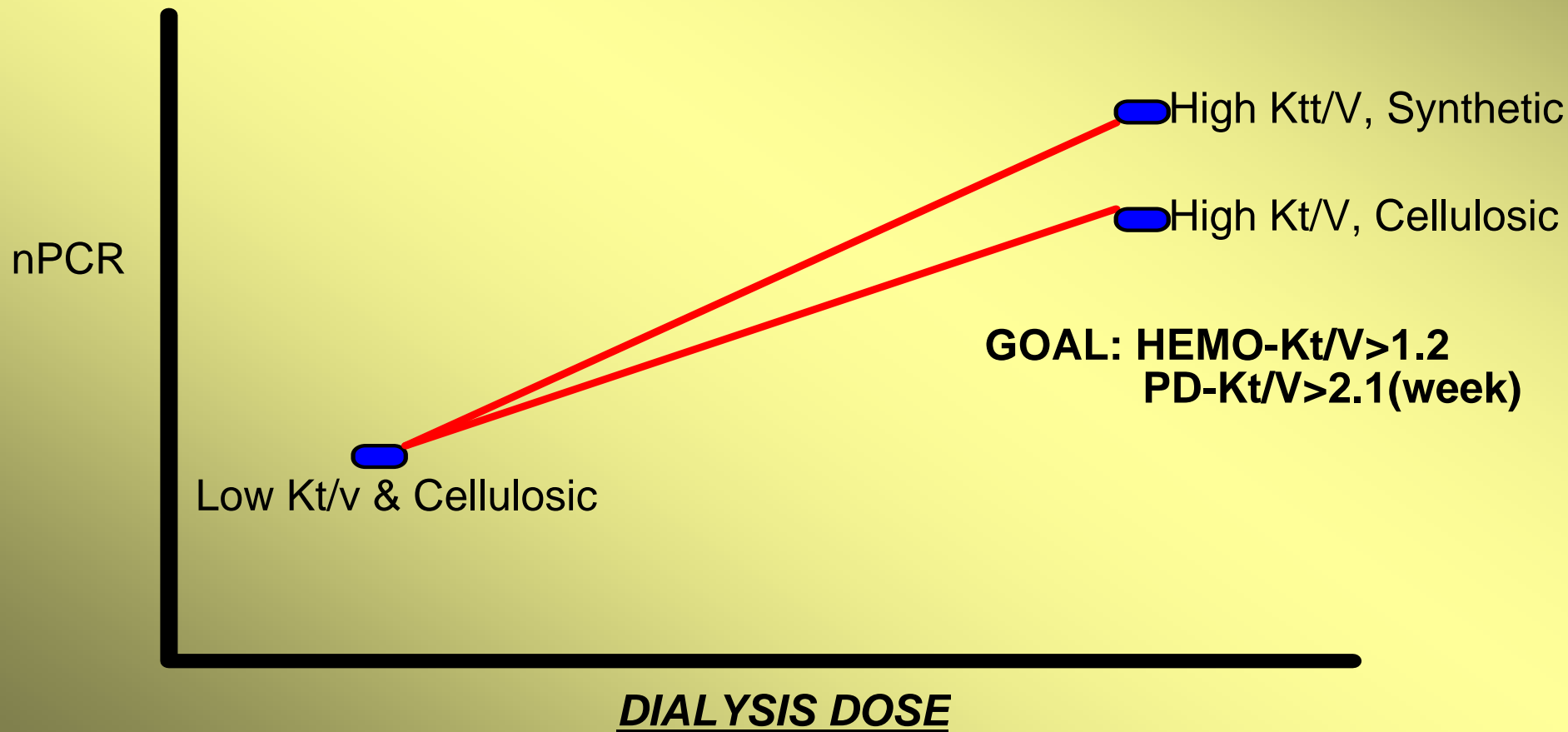


USRDS Case Mix Adequacy Study, 1990/91, n = 2,410

MEMBRANE FLUX: A POTENTIAL CONFOUNDING VARIABLE

- CHANGES IN K_t/V WERE IN PART ACCOMPLISHED BY USE OF HFM
- POTENTIAL BENEFITS OF HFM
 - IMPROVED PROTEIN CATABOLIC RATE
 - IMPROVED TG METABOLISM
 - IMPROVED EPO RESPONSE
 - IMPROVED BETA₂-MICROGLOBULIN REMOVAL
- HOWEVER, BECAUSE OF LOW T_D , THE FULL EFFECT OF HFM IS NOT EVIDENT. REMOVAL OF HIGH MW SUBSTANCES ARE ALSO TIME DEPENDENT.

INFLUENCE OF DOSE AND DIALYZER CHOICE ON NUTRITION



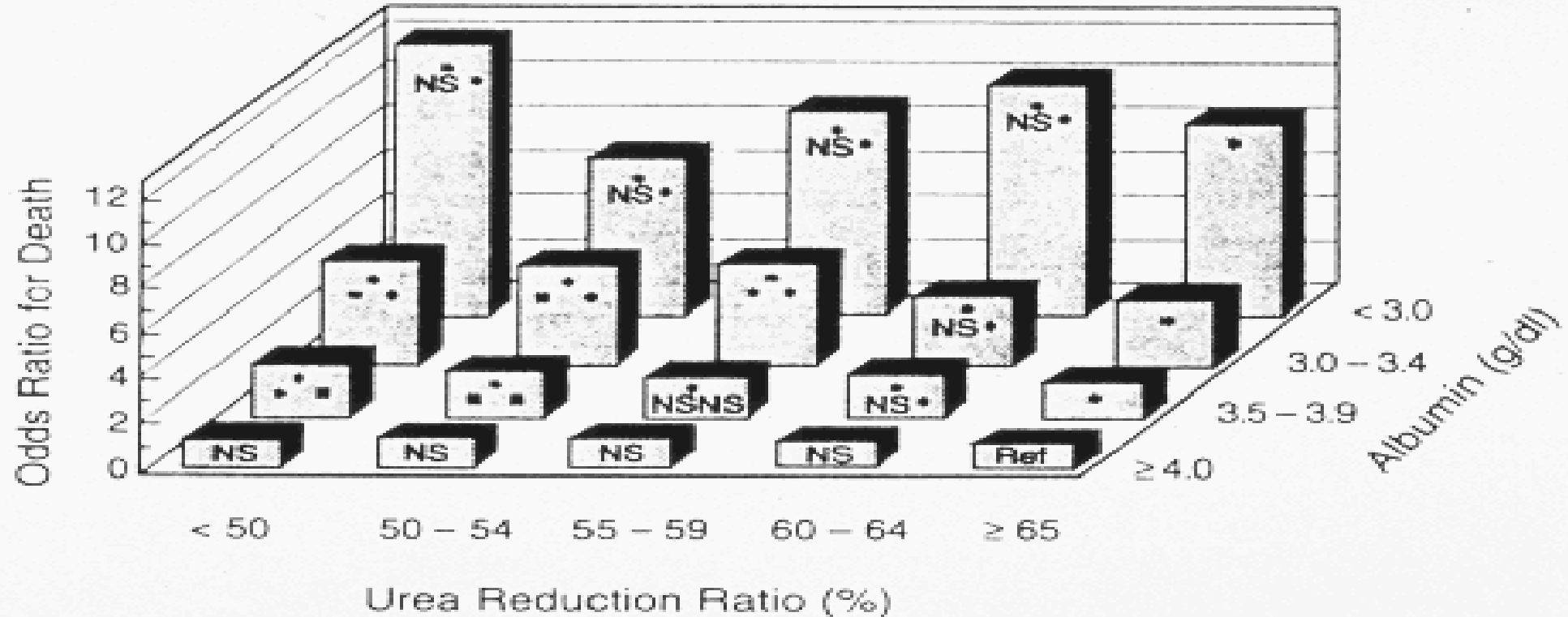
ADEQUACY AND NUTRITIONAL STATUS

NUTRITIONAL PARAMETERS AND YEARLY AVERAGE KT/V VUMC Dialysis Patients

<u>N</u>	<u>Yearly Average Kt/V</u>	<u>Albumin</u>	<u>Transferrin</u>	<u>PCR</u>
16	< 0.86	3.5 ± 0.3	220 ± 34	0.83 ± 0.19
16	> 1.21	3.9* ± 0.2	257* ± 64	1.00* ± 0.19

* P < 0.05

ADEQUACY AND ALBUMIN LEVEL



HEMODIALYSIS TIME: THE UNRESOLVED PARAMETER

- K_D IS A MERE TECHNICAL ISSUE
- MINIMUM T_D HAS ITS BASIS ROOTED IN PHYSIOLOGY
- SHORT TIME MAKES HEMODIALYSIS UNFORGIVING:

Prescribed Kt/V	Calculated Kt/V	Delivered Kt/V
1.56 ± 0.28	1.50 ± 0.28	1.37 ± 0.23

- EXCEPT FOR TASSIN, NO MODERN STUDIES HAS EXAMINED LONG (>5 HOURS) TIME AND OUTCOME

THE NCDS POPULATION

Table 5. NCDS Inclusion/Exclusion

Age, 18-70 years (mean, 49.0 ± 12.7)
(US 1988 mean, 57 years)
(US 1988 median, 60 years)
Average time on dialysis, 4.2 ± 2.3 years
No diabetes
(1988 US acceptance rate, 30%)
No malignancy
No significant cardiovascular disease
No hospitalization for past 6 months
T_d range, 2.5-5.5 hours during study
(mean before participation, 4.3 hours)
Cooperative
Compliant

FACTORS RELATED TO DIALYSIS ADEQUACY

- **HEMODIALYSIS
RELATED FACTORS**

- DOSE

- LOW MW SOLUTES
- HIGH MW SOLUTES
- DIALYSIS TIME

- **MEMBRANE**

- FLUX
- BIOCOMPATIBILITY
- REUSE

- **PATIENT RELATED
FACTORS**

- NUTRITION

- ACIDOSIS

- CA x P

- BLOOD PRESSURE

- LIPIDS

- CARDIOVASCULAR
MORBIDITY

- INFLAMMATION

ALTERNATIVES FOR THE HEMO STUDY

HEMO STUDY

Choice

- Dialysis Dose
- Dialysis Time
- Biocompatibility
- Flux
- Nutrition

Controversy

- We know the answer
- Does not reflect U.S. practice
- Confounded by reuse techniques
- Definition
- Prohibitive cost

Remember: Limited Funds Dictates 2 x 2 Design

THE HEMODIALYSIS (HEMO) STUDY

AN NIH-NIDDK SPONSORED
RANDOMIZED, MULTI-CENTER
CLINICAL TRIAL

THE CHOICE: OBJECTIVES OF THE HEMO STUDY

In patients undergoing 3x/week maintenance hemodialysis, to determine whether

higher dose, or

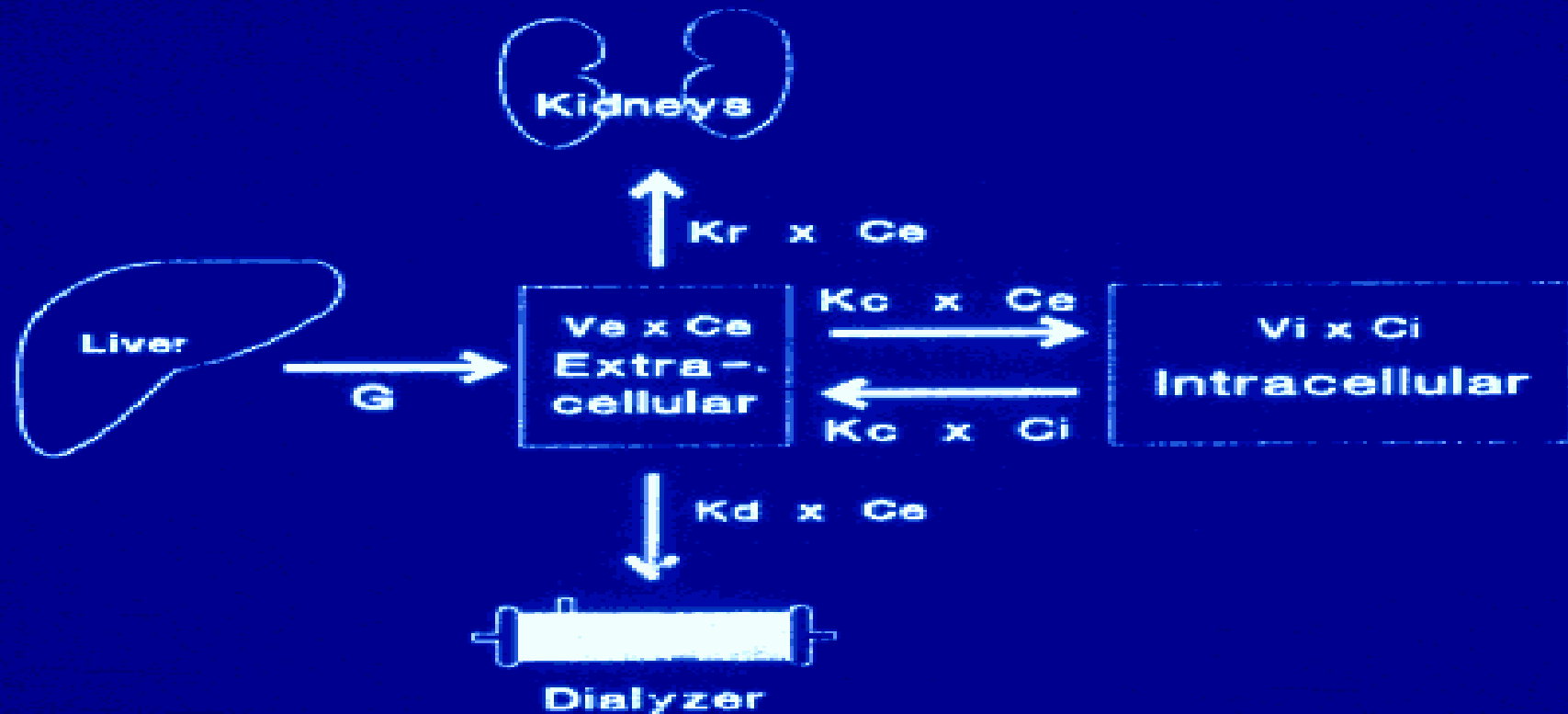
high-flux membrane

affect

mortality (primary outcome), or

morbidity (secondary outcome)

DOUBLE POOL KINETICS



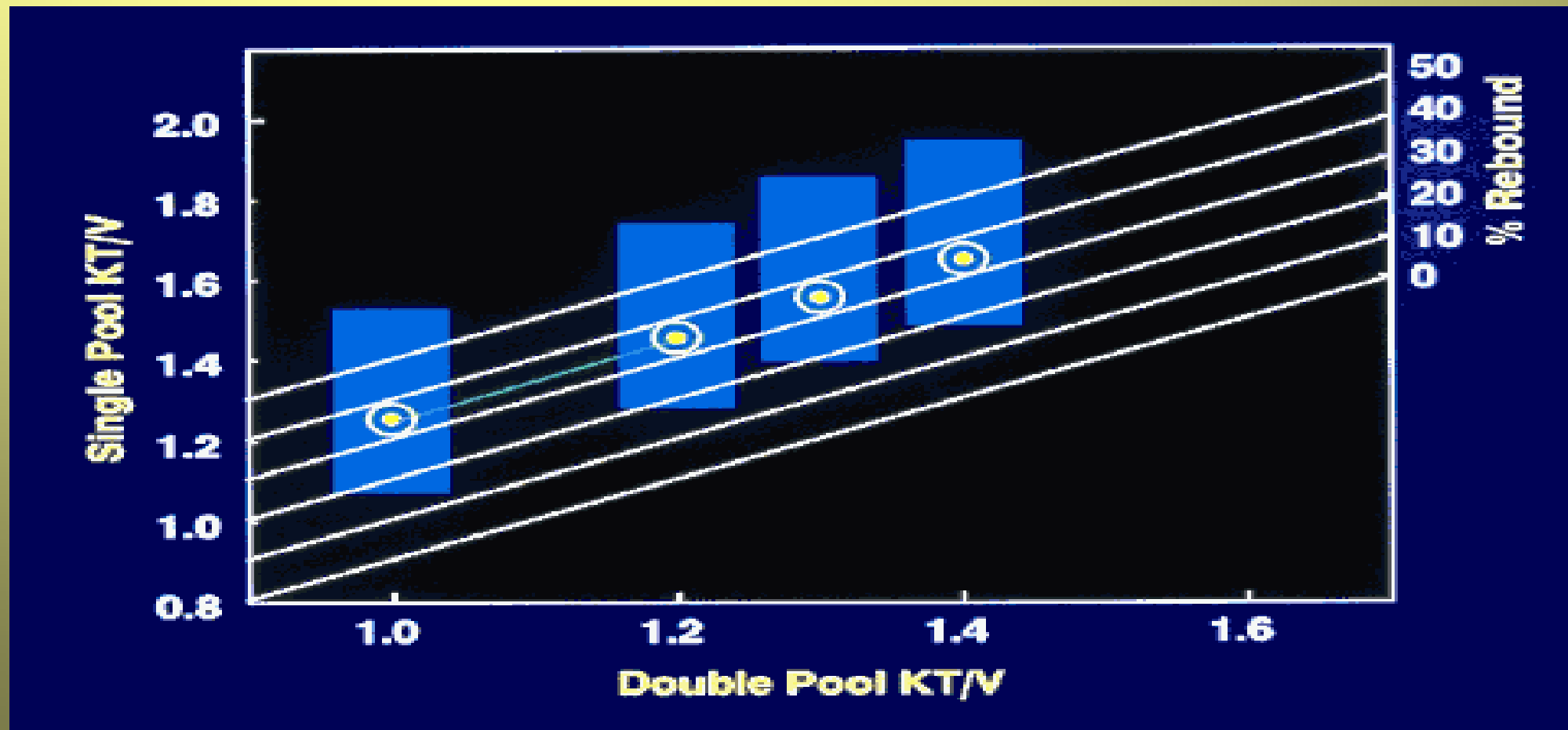
THE RATE EQUATION

Rate equation

$$eKt/V = spKt/V - 0.6(K/V) + 0.03$$

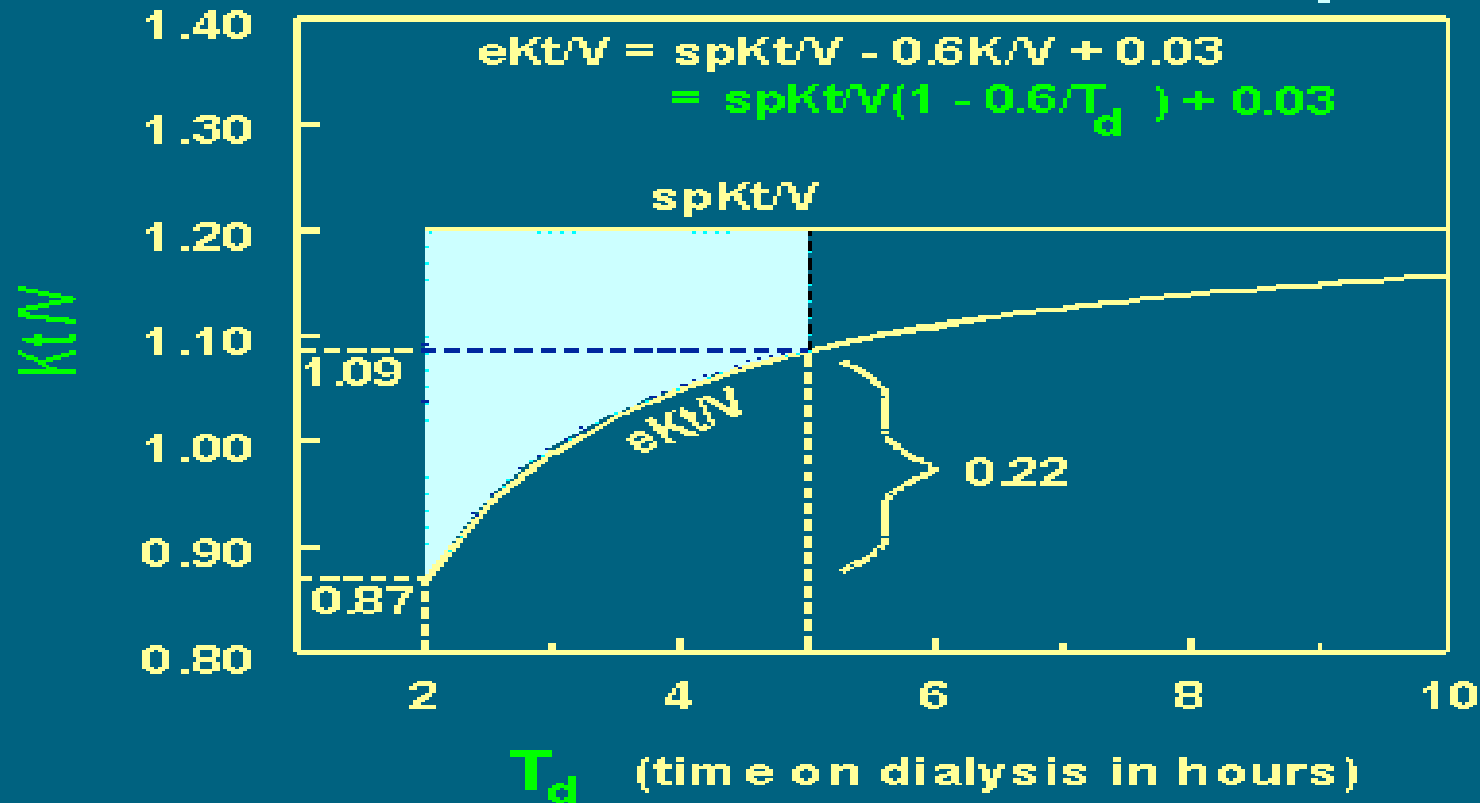
(K/V in hours⁻¹)

RELATIONSHIP OF Kt/V_{SP} TO Kt/V_{DP} AND AS A FUNCTION OF REBOUND

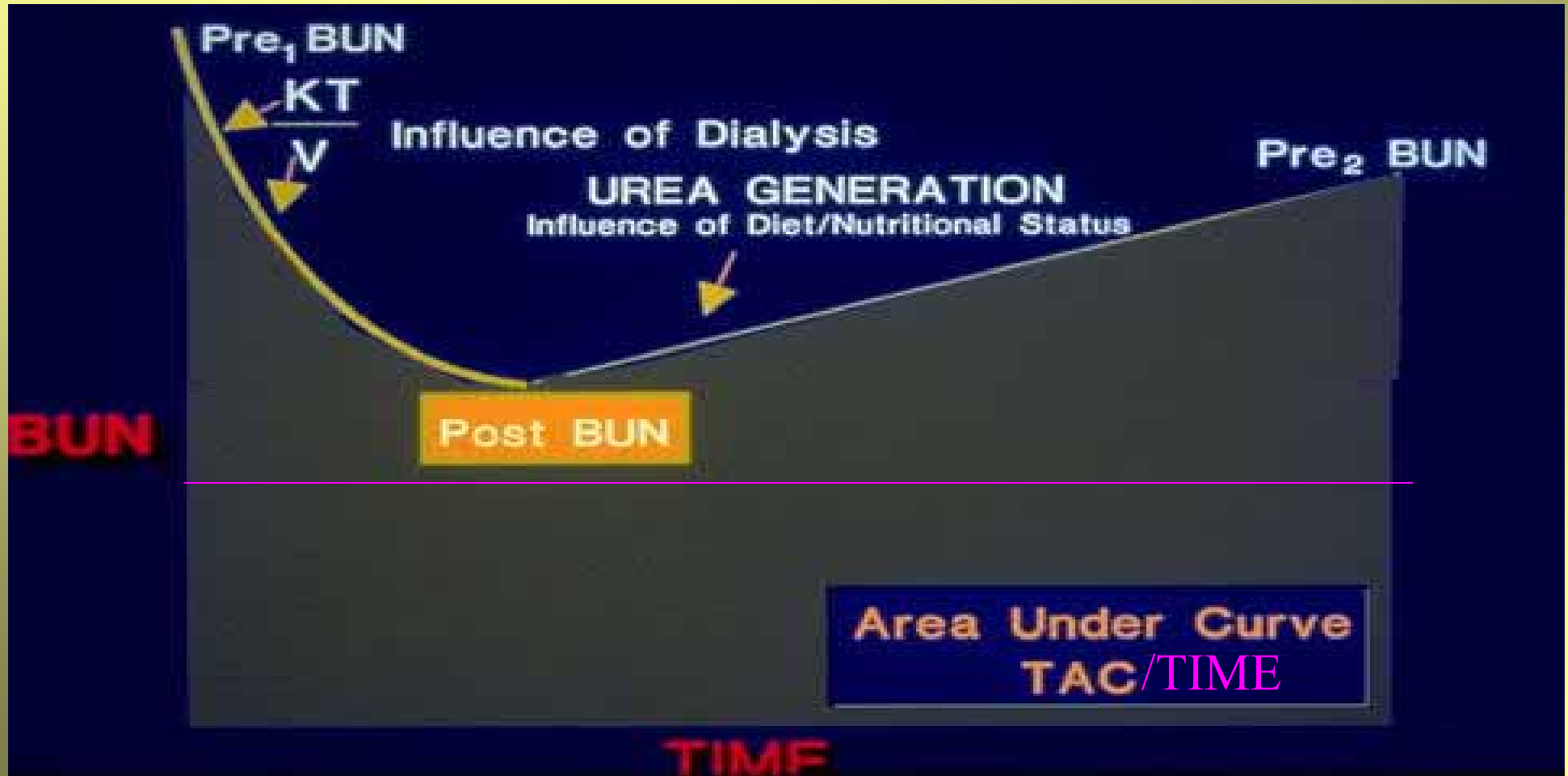


RATE EQUATION AS A FUNCTION OF TIME

Predictions of the Rate Equation



THE DIALYSIS CYCLE



Dose

Standard dose

$$eKt/V = 1.05$$

$$spKt/V \approx 1.25$$

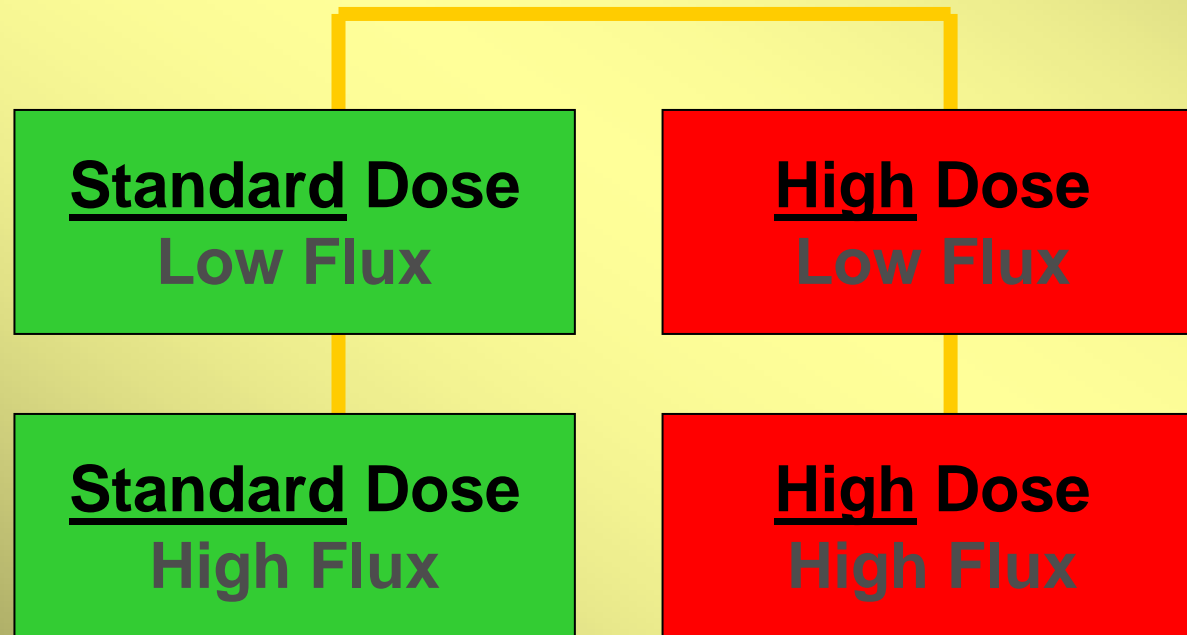
$$URR \approx 65\%$$

High dose

$$eKt/V = 1.45$$

$$spKt/V \approx 1.65$$

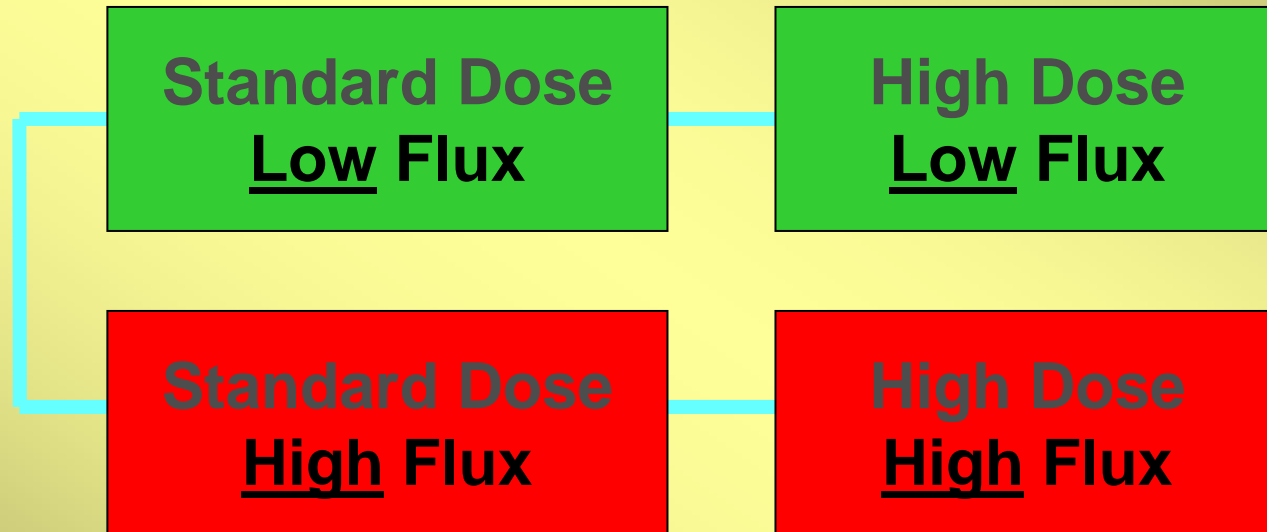
$$URR \approx 75\%$$



Flux

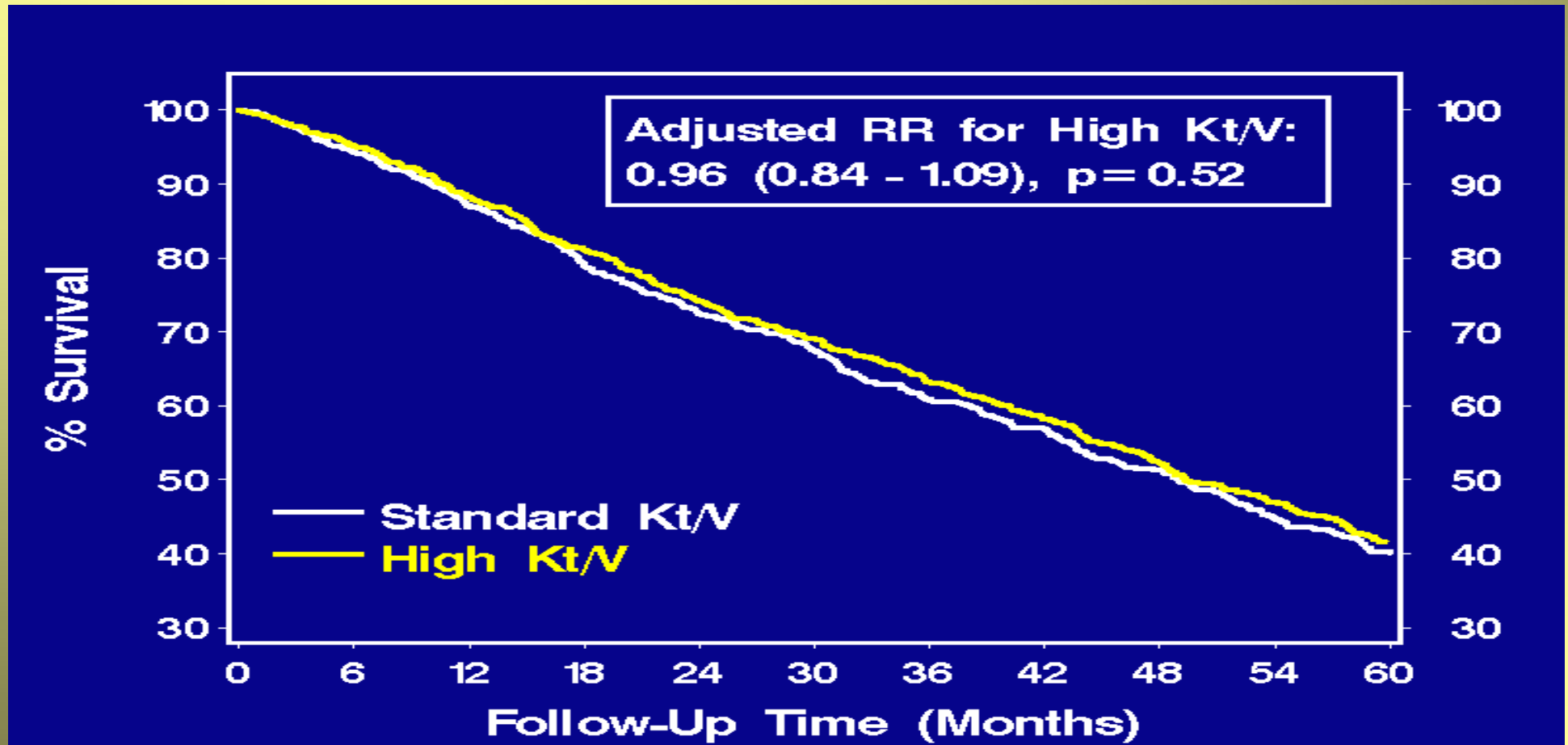
Low-flux dialyzers: β_2 M clearance < 10 ml/min

Flux
comparison

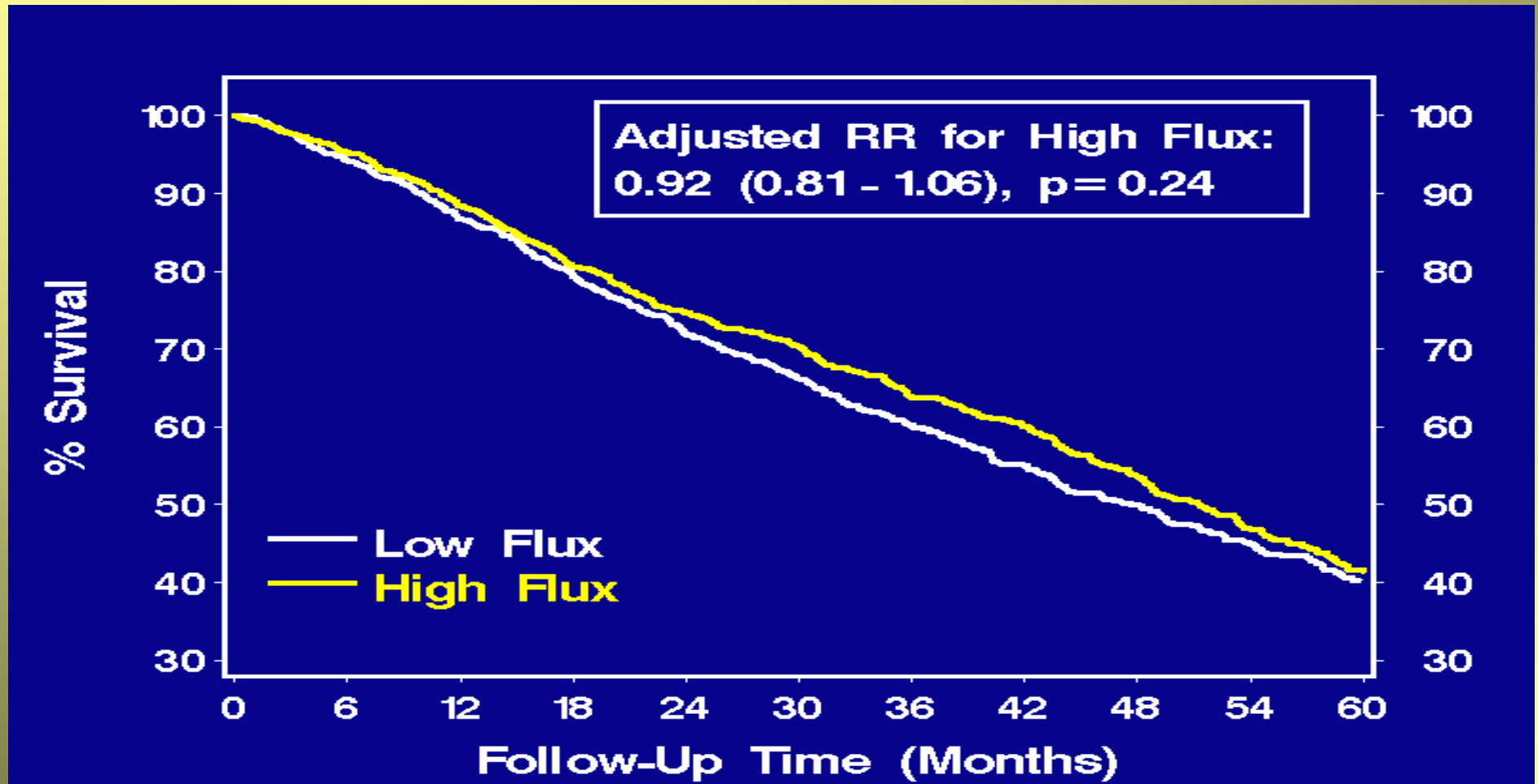


High-flux dialyzers: β_2 M clearance > 20 ml/min

Time to Death by Kt/V Group



Time to Death by Flux Group



Interactions of Treatments with Baseline Characteristics

**Did treatment effects differ between
subgroups for seven pre-specified
baseline factors?**

Age

Gender

Race

Diabetes

Years of dialysis

Comorbidity

Albumin

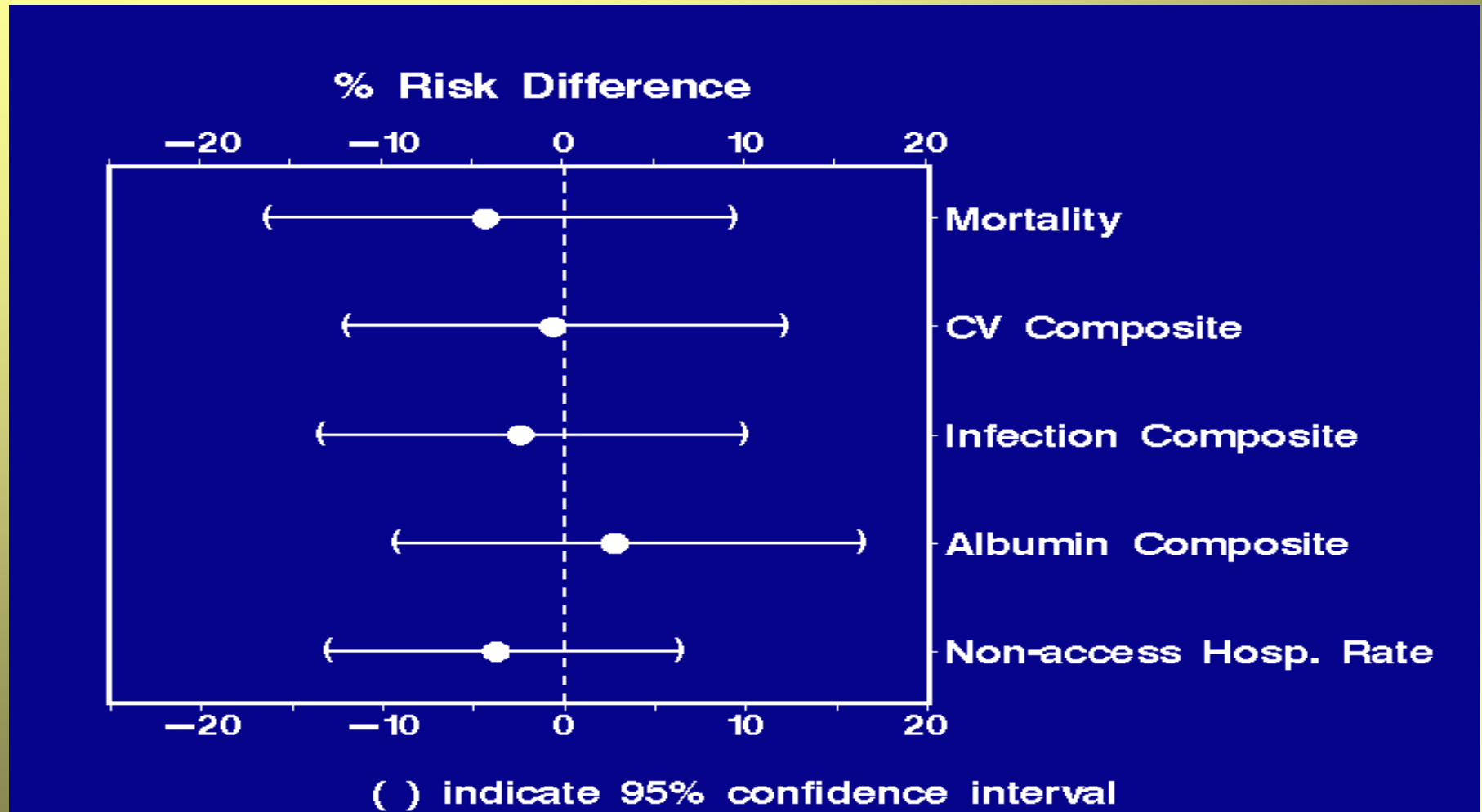
Predictors of Mortality by Cox Regression

Predictor Variable	Relative Risk	95% Confidence	p-value
High dose	0.96	(0.84, 1.09)	0.52
High flux	0.92	(0.81, 1.06)	0.24
Age (per 10 yrs increase)	1.44	(1.35, 1.54)	<0.001
Gender (female)	0.86	(0.74, 0.99)	0.03
Race (African American)	0.76	(0.65, 0.89)	0.001
Diabetes	1.24	(1.06, 1.45)	<0.001
Years of dialysis	1.04	(1.02, 1.06)	<0.001
Baseline serum albumin (per 0.5 g/dL increment)	0.51	(0.43, 0.62)	<0.001

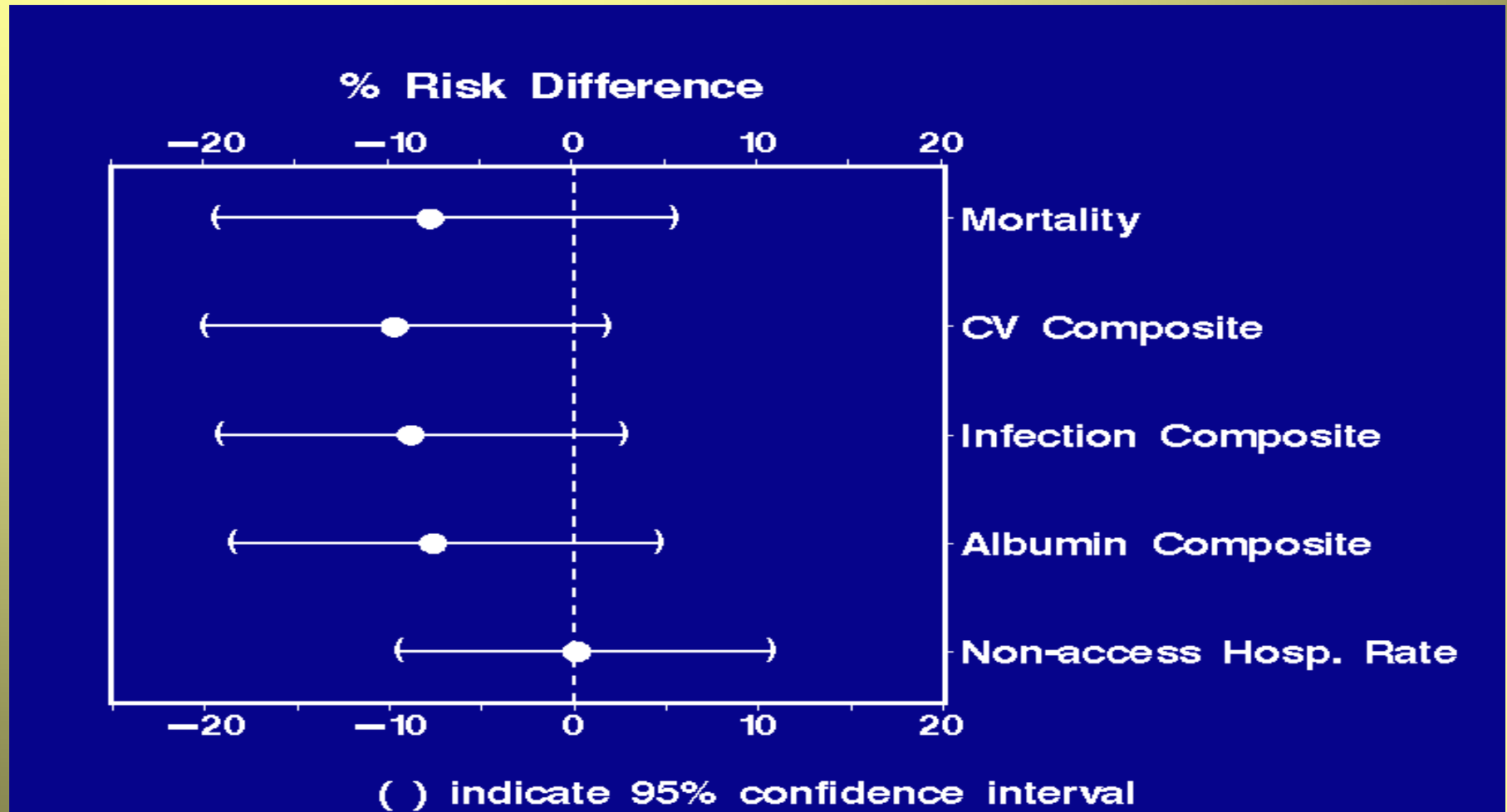
Model also includes 2 other sig. variables: ICED, albumin x time

Analysis stratified by clinical center

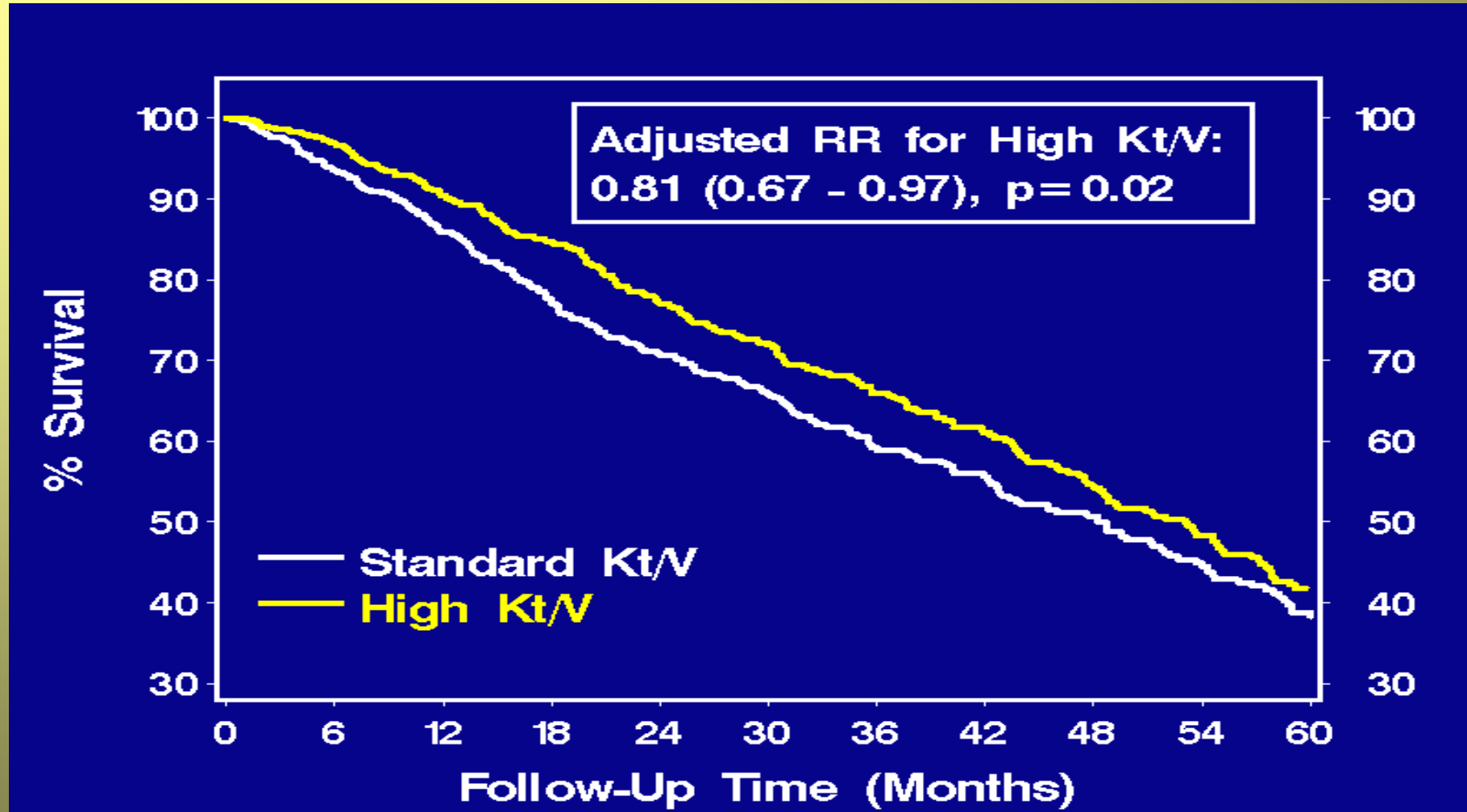
Effect of High Dose on Primary and Pre-specified Secondary Outcomes



Effect of High Flux on Primary and Pre-specified Secondary Outcomes

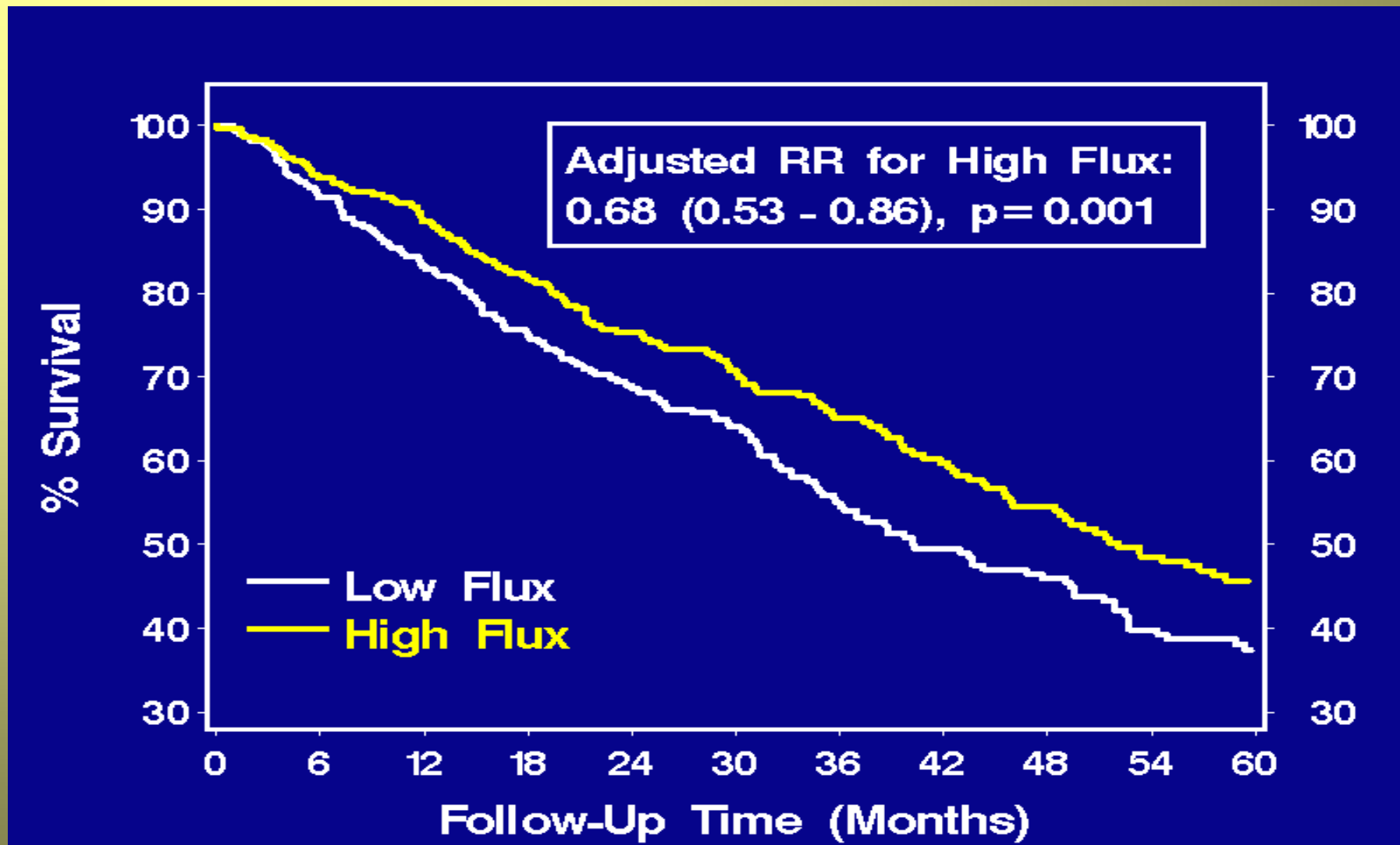


Time to Death by Kt/V Group Females (484 Deaths)

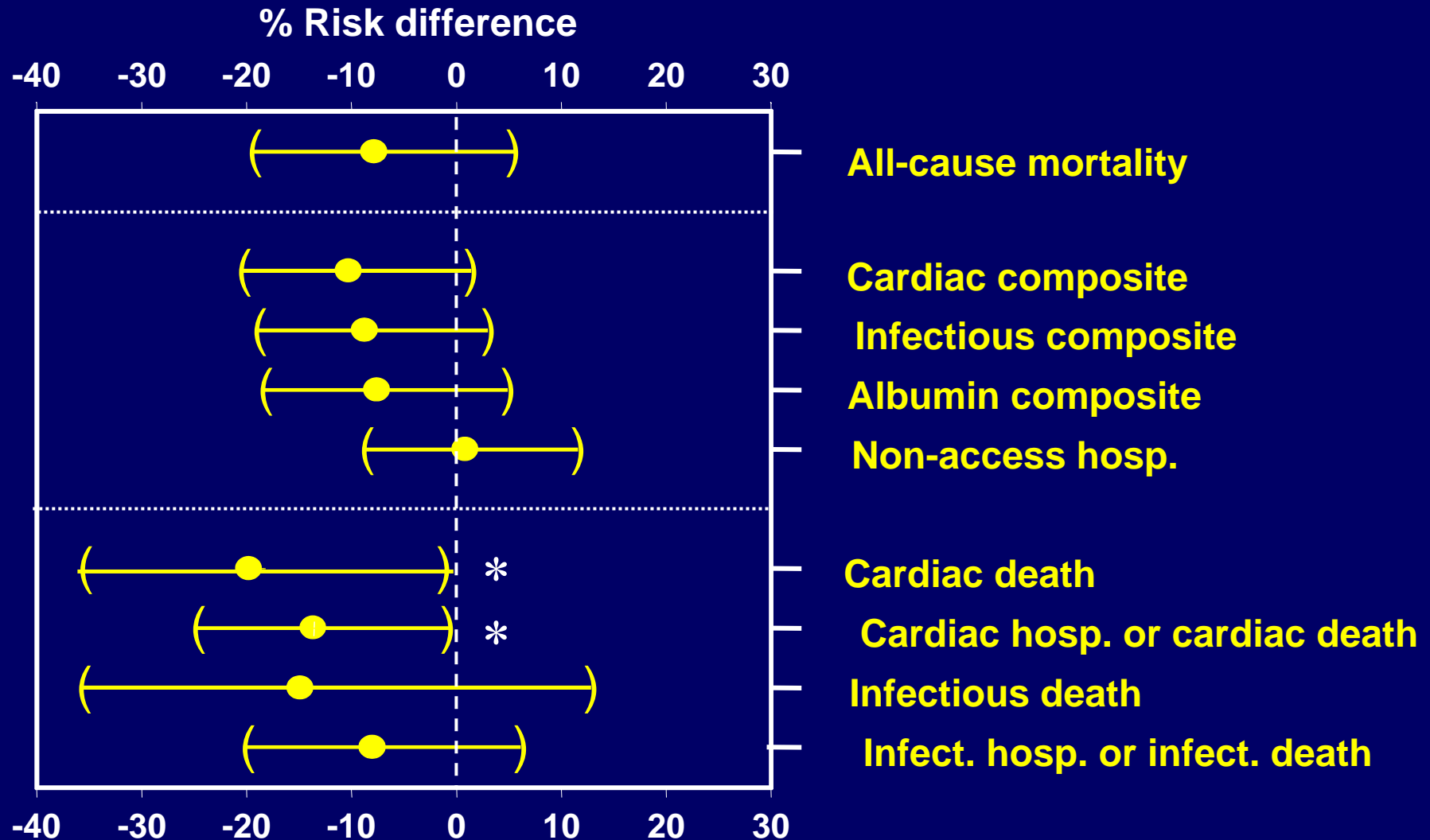


Time to Death by Flux Group

Duration of Dialysis > 3.7 Years (298 Deaths)



Effects of High Flux on Primary and Secondary Outcomes



() indicate 95% confidence interval

HEMO STUDY SUMMARY

1) THE HIGHER DOSE OF HEMODIALYSIS THRICE WEEKLY DID NOT:

**IMPROVE SURVIVAL,
REDUCE HOSPITALIZATIONS, OR
MAINTAIN SERUM ALBUMIN**

2) USE OF A HIGH FLUX MEMBRANE DID NOT:

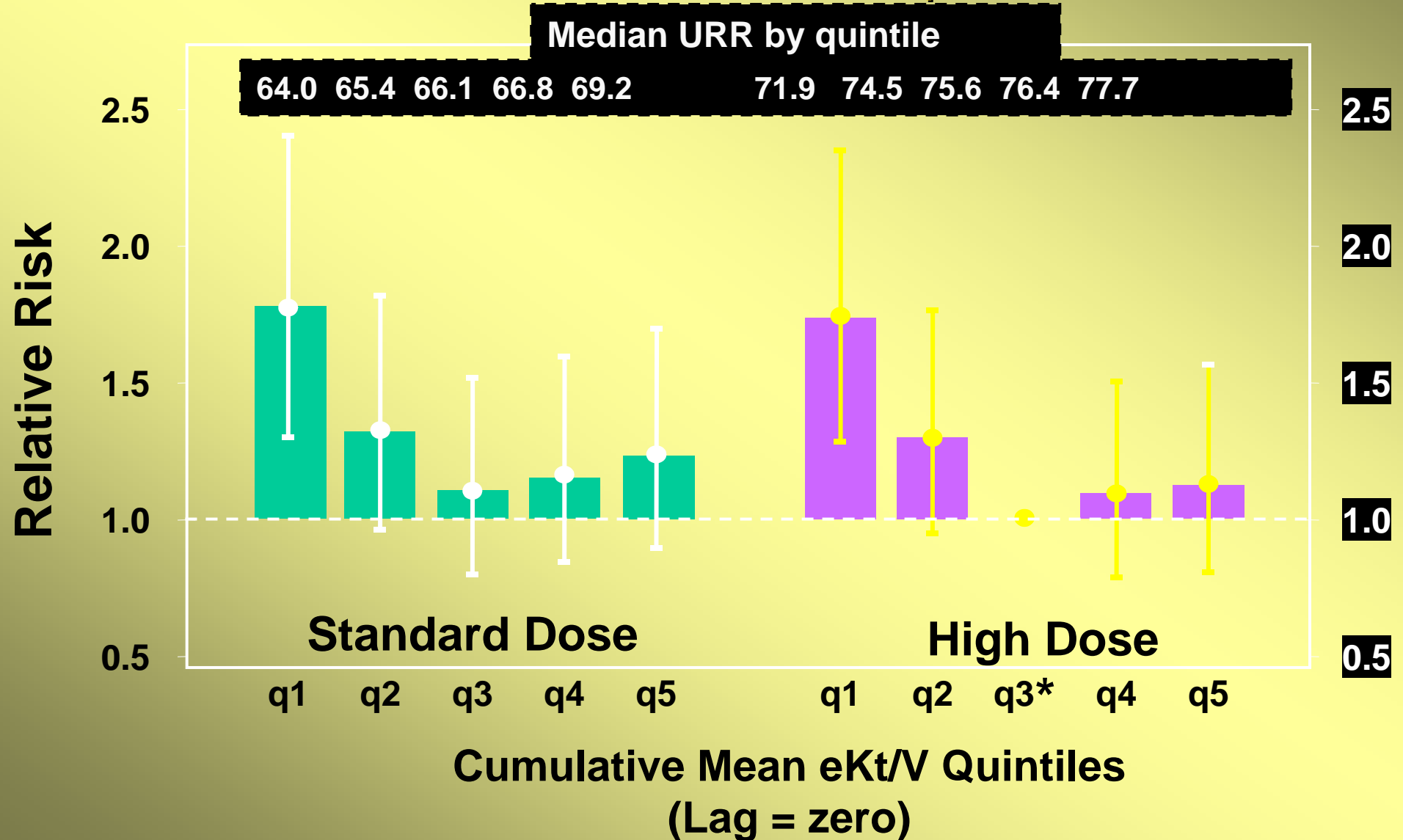
**IMPROVE SURVIVAL,
REDUCE HOSPITALIZATIONS, OR
MAINTAIN SERUM ALBUMIN**

HEMO STUDY SUMMARY

3) HOWEVER, EFFECTS MAY VARY AMONG CERTAIN SUBSETS OF PATIENTS:

- A) IN WOMEN, THE HIGHER DOSE OF DIALYSIS MAY BE ASSOCIATED WITH INCREASED SURVIVAL**
- B) IN PATIENTS WITH > 3.7 YEARS ON DIALYSIS, USE OF A HIGH FLUX MEMBRANE MAY BE ASSOCIATED WITH INCREASED SURVIVAL**
- C) THE RESULTS ON THESE SUBSETS SHOULD BE INTERPRETED CAUTIOUSLY AND BE FURTHER INVESTIGATED**

Relative Risk of Mortality vs. Mean Achieved eKt/V Within Dose Groups



* Reference Group

MORTALITY BY ACHIEVED DOSE

◀ DOSE TARGETING SELECTION BIAS ▶

- IN THE SETTING OF INTENSE DOSE TARGETING A STRONG SELECTION BIAS WAS APPARENT, I.E., PATIENTS WITH CONDITIONS PREDISPOSING TO DEATH TENDED ALSO TO HAVE LOWER eKT/V RELATIVE TO THEIR TARGETED DOSE.
- SIMILAR TRENDS WERE FOUND WITHIN BOTH RANDOMIZED DOSE GROUPS.
- THIS COULD NOT BE EXPLAINED ON THE BASIS OF A TRUE DOSE EFFECT.
- THE CAUSE(S) REMAIN(S) SPECULATIVE; ASSOCIATION OF ACCESS DIFFICULTIES WITH LOWER-THAN-TARGET ACHIEVED DOSES ACCOUNTS FOR SOME OF THIS EFFECT.

PATIENT AND TREATMENT EFFECTS ASSOCIATED WITH COMPARATIVELY LOW ACHIEVED EKT/V

- FACTORS ASSOCIATED WITH LOWER ACHIEVED EKT/V AND HIGHER MORTALITY :
 - INCREASE IN KINETIC VOLUME
 - VENOUS CATHETERS
 - ACCESS PROCEDURES
 - HOSPITALIZATIONS
 - DECLINE IN SERUM ALBUMIN
 - REDUCTION IN TREATMENT TIME
- STRONGER IN HIGH DOSE GROUP, BUT OBSERVED IN STANDARD DOSE AS WELL

DOSE TARGETING SELECTION BIAS - IMPLICATIONS FOR OBSERVATIONAL STUDIES

- MAGNITUDE OF DOSE TARGETING BIAS SEEN HERE IS MUCH GREATER THAN EFFECTS OF ACHIEVED EKT/V IN OBSERVATIONAL STUDIES
- WIDER RANGE OF TARGET DOSES, LESS INTENSE DOSE TARGETING, IN OBSERVATIONAL STUDIES
- HYPOTHESIS: BIAS DUE TO DOSE-TARGETING EFFECT MAY MAKE IT DIFFICULT TO ANSWER THE QUESTION, “WHAT IS THE OPTIMAL DIALYSIS DOSE?” BY CROSS-SECTIONAL STUDIES

ARE WE CONFOUNDING DETERMINATION OF ADEQUACY BY THE USE OF Kt/V ?

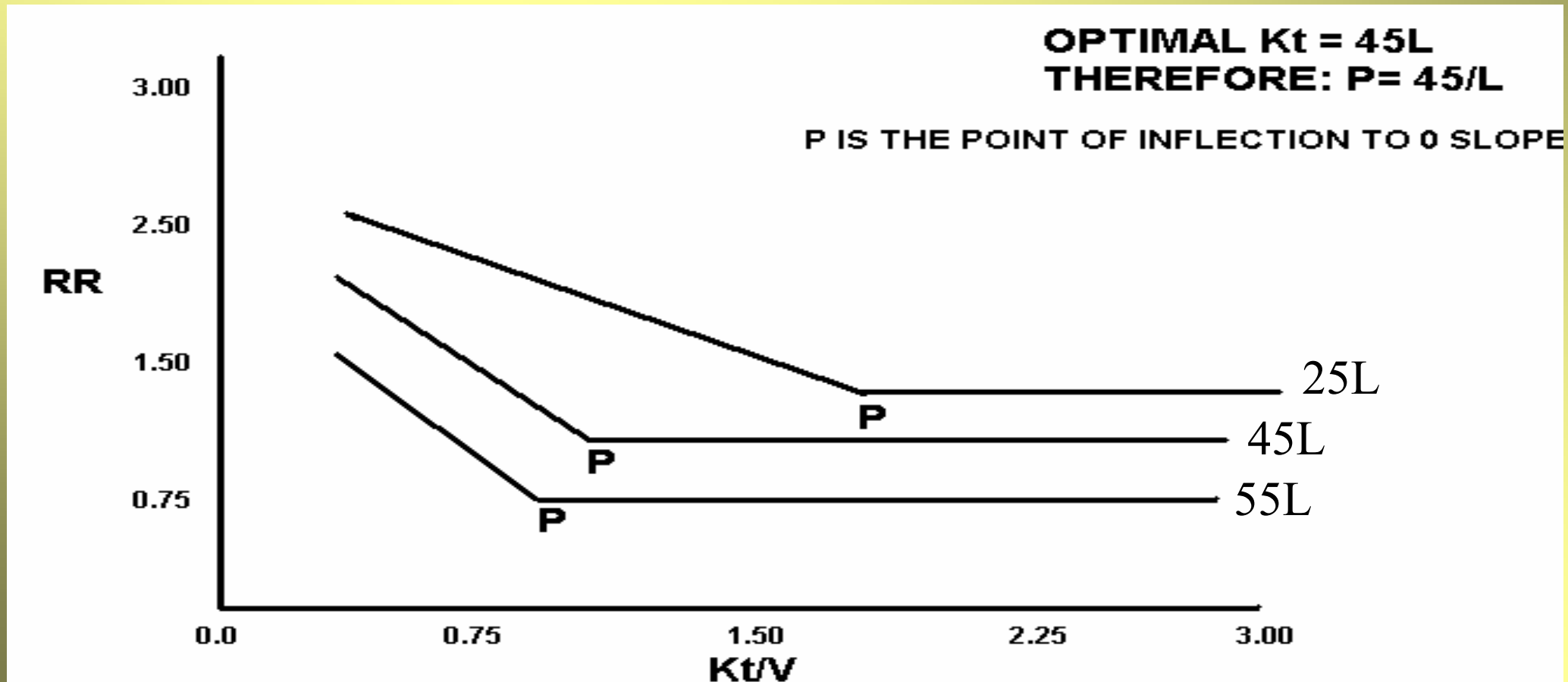
Kt/V

Kt = AMOUNT OF DIALYSIS, A GOOD THING

V = VOLUME~WEIGHT~MUSCLE MASS, A GOOD THING

A GOOD THING/A GOOD THING

UREA VOLUME AND SURVIVAL



RELATIVE RISK OF DEATH

MINEFIELDS AVOIDED BY THE HEMO STUDY

- **DESPITE ITS LENGTH, WE AVOIDED BEING ECLIPSED BY CHANGES IN COMMUNITY PRACTICE PATTERNS**
 - **T_D , Q_B , Q_D SIMILAR TO USRDS**
 - **MEMBRANES SIMILAR**
 - **STANDARD LEVEL Kt/V DELIVERED WAS BETTER OR EQUAL TO COMMUNITY PRACTICE THROUGHOUT THE STUDY. THE COMMUNITY RECOMMENDATIONS EXCEEDED HEMO STANDARD Kt/V FOR ONLY A SHORT TIME**
- **DOSE AND FLUX GOALS ACHIEVED**
- **MORTALITY NOT OVERESTIMATED**
- **ADEQUATELY POWERED**
- **WHAT WAS PILOTED *IS* WHAT WAS STUDIED**

WHY THE HEMO STUDY WAS NEEDED

- **RAPIDLY GROWING ESRD POPULATION**
 - 10 %/YEAR GROWTH RATE, COSTING \$BILLIONS
 - WORSENING COMORBIDITY
 - MAJORITY TREATED BY HEMODIALYSIS
- **US ANNUAL GROSS MORTALITY OF 21-23%**
- **OBSERVATIONAL AND CORRELATIONAL STUDIES
DEMONSTRATING IMPROVED SURVIVAL FOLLOWING
TREATMENT CHANGES**
 - HIGHER DOSE AS MEASURED BY Kt/V OR URR
 - BIOCOMPATIBLE MEMBRANES
 - REMOVAL OF HIGH MW SUBSTANCES (FLUX)

IMPLICATIONS OF THE HEMO STUDY

What situations require clinical guidelines to be updated?

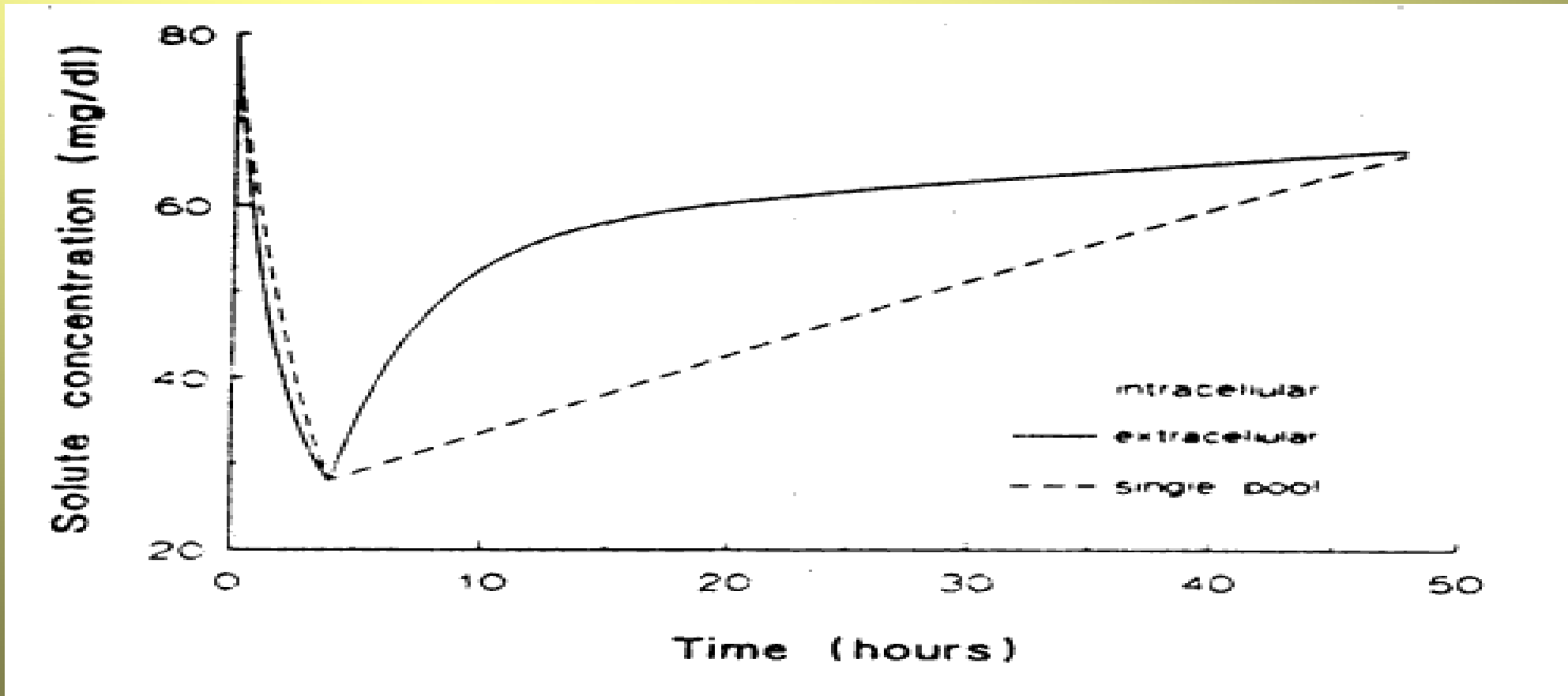
- **Changes in evidence on the existing benefits and harms of interventions**
- **Changes in outcomes considered important**
- **Changes in available interventions**
- **Changes in evidence that current practice is optimal**
- **Changes in values placed on outcomes**
- **Changes in resources available for health care**

BMJ 2001;323:155-157

PLACES TO GO NEXT

- **Changing a number?**
- **Changing an approach:**
 - Cardiovascular Risk Reduction
 - Control of Co-morbid Conditions
 - Solute Removal: beyond small solutes
 - Volume Control
 - Nutrition
 - Anemia Correction
 - Bone Disease

LARGE MOLECULE REBOUND



MEMBRANE FLUX: A POTENTIAL CONFOUNDING VARIABLE

- CHANGES IN Kt/V WERE IN PART ACCOMPLISHED BY USE OF HFM
- POTENTIAL BENEFITS OF HFM
 - IMPROVED PROTEIN CATABOLIC RATE
 - IMPROVED TG METABOLISM
 - IMPROVED EPO RESPONSE
 - IMPROVED BETA₂-MICROGLOBULIN REMOVAL
- HOWEVER, BECAUSE OF LOW T_D , THE FULL EFFECT OF HFM IS NOT EVIDENT: **REMOVAL OF HIGH MW SUBSTANCES ARE ALSO TIME DEPENDENT- LONGER TIMES ARE NECESSARY TO SHOW BENEFITS OF HFM**

HEMODIALYSIS TIME: THE UNRESOLVED PARAMETER

- K_D IS A MERE TECHNICAL ISSUE
- MINIMUM T_D HAS ITS BASIS ROOTED IN PHYSIOLOGY
- SHORT TIME MAKES HEMODIALYSIS UNFORGIVING:

Prescribed Kt/V	Calculated Kt/V	Delivered Kt/V
1.56 ± 0.28	1.50 ± 0.28	1.37 ± 0.23

- EXCEPT FOR TASSIN, NO MODERN STUDIES HAS EXAMINED LONG (>5 HOURS) TIME AND OUTCOME

POTENTIAL PARAMETERS TO CONSIDER WITH NOCTURNAL AND DAILY HD

IS IT INCREASED TIME OR INCREASED QUANTITY?

FACTORS THAT MAY INFLUENCE MORBIDITY AND SURVIVAL ON HEMODIALYSIS

- MEMBRANES: SYNTHETIC, FLUX
- DIALYSATE: SODIUM, BICARBONATE
- PHOSPHATE, Ca x P, Ca
- EPO
- DIALYSIS KINETICS
- DIALYSIS TIME
- NUTRITION

The diagram illustrates the relationship between various factors and alternate dialysis schedules. A large blue arrow points from the list of factors to a box containing the text 'ALTERNATE DIALYSIS SCHEDULES'. Additionally, blue lines connect specific factors to the box: 'MEMBRANES: SYNTHETIC, FLUX' and 'PHOSPHATE, Ca x P, Ca' are connected by horizontal lines that meet a vertical line descending to the box; 'EPO' is connected by a horizontal line that meets the same vertical line; 'DIALYSIS KINETICS' is connected by a large blue arrow pointing directly to the box; and 'NUTRITION' is connected by a horizontal arrow pointing directly to the box.

**ALTERNATE
DIALYSIS
SCHEDULES**

ISSUES TO BE CONSIDERED

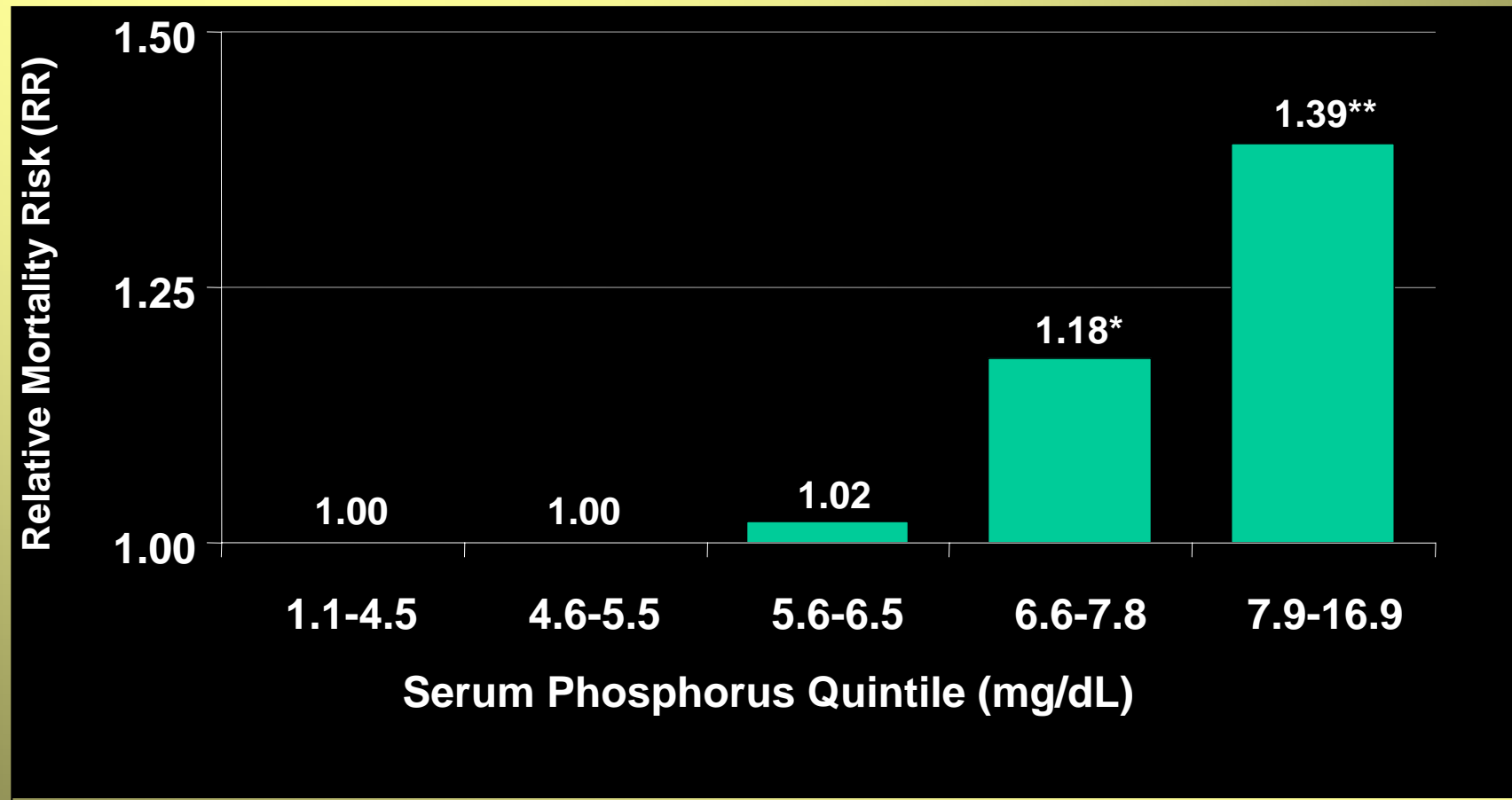
- **DEFINITIONS OF THE MODALITIES**
- INDIVIDUAL STUDIES OF EACH OF THE MODALITIES
- DAILY HEMODIALYSIS vs NOCTURNAL HEMODIALYSIS

ALTERNATIVES TO STANDARD HEMODIALYSIS TREATMENTS

- SLOW LONG-DURATION HEMODIALYSIS
 - THRICE WEEKLY; BIOINCOMPATIBLE MEMBRANE; 6-8 HOURS; $Q_B = 200-220$ mL/min; $Kt/V > 1.8$
- SHORT DURATION DAILY DIALYSIS
 - 5-6 TIMES EACH WEEK; HIGH FLUX BIOCOMPATIBLE MEMBRANE ; 1.5-2.5 HOURS; $Q_B > 400$ mL/min; $Kt/V .2-.8$
- NOCTURNAL HEMODIALYSIS
 - 5-7 TIMES EACH WEEK; BIOCOMPATIBLE MEMBRANE; 6-8 HOURS; $Q_B = 250-300$ mL/min; $K .9-1.2$

Elevated Serum Phosphorus

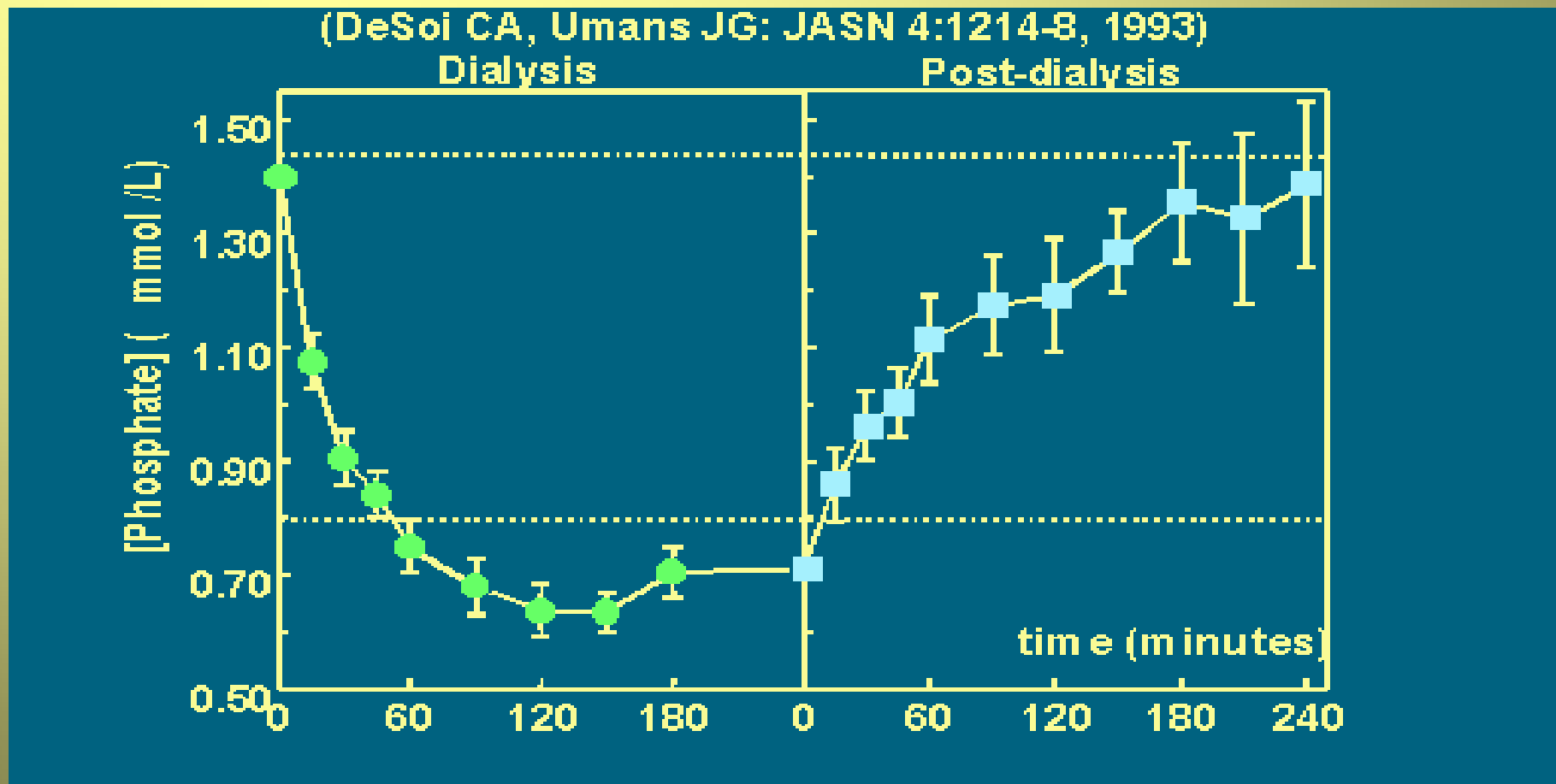
Increases Mortality Risk¹ { US PTS 39% > 6.5 }



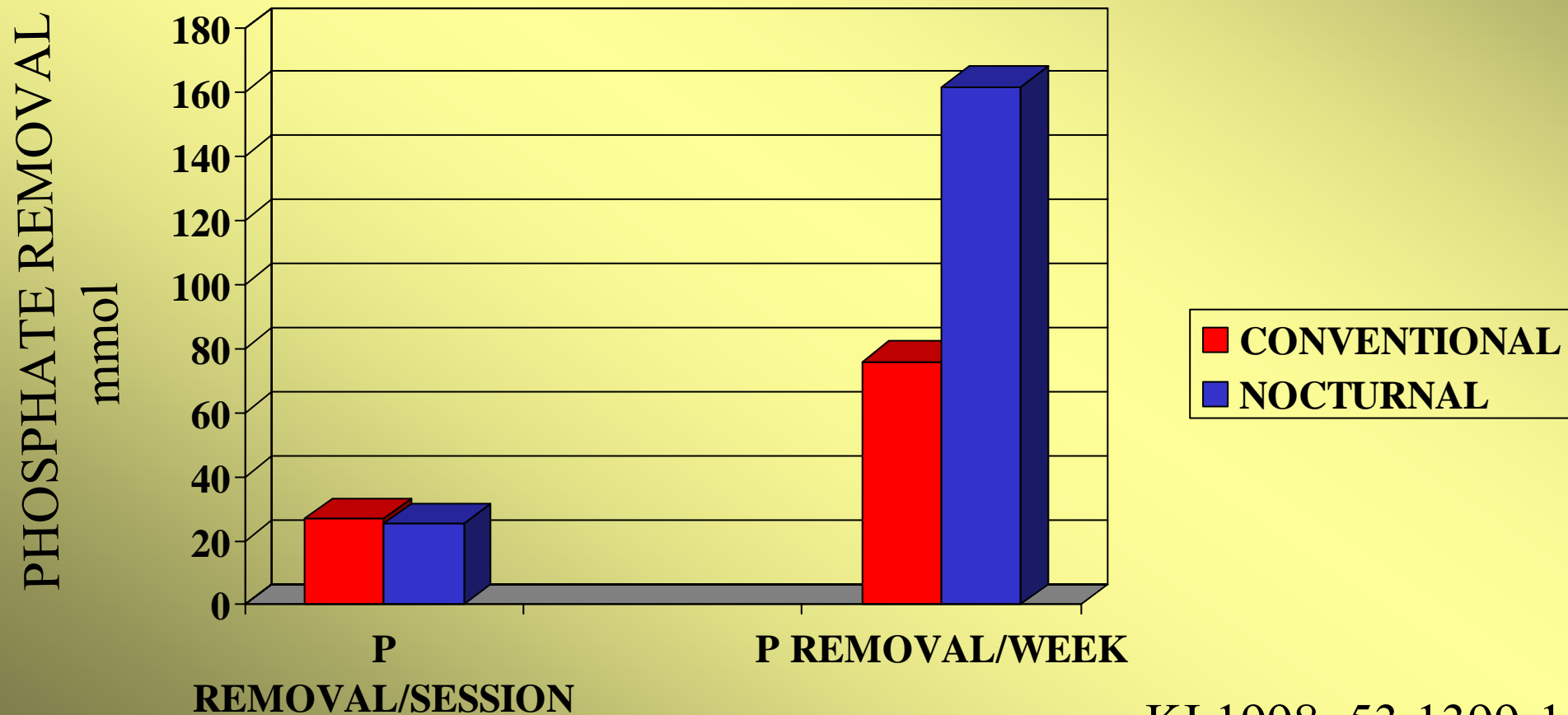
*P=0.03 **P<0.0001 (n=6407)

1. Adapted from Block GA, et al. *Am J Kidney Dis.* 1998;31:607-617.

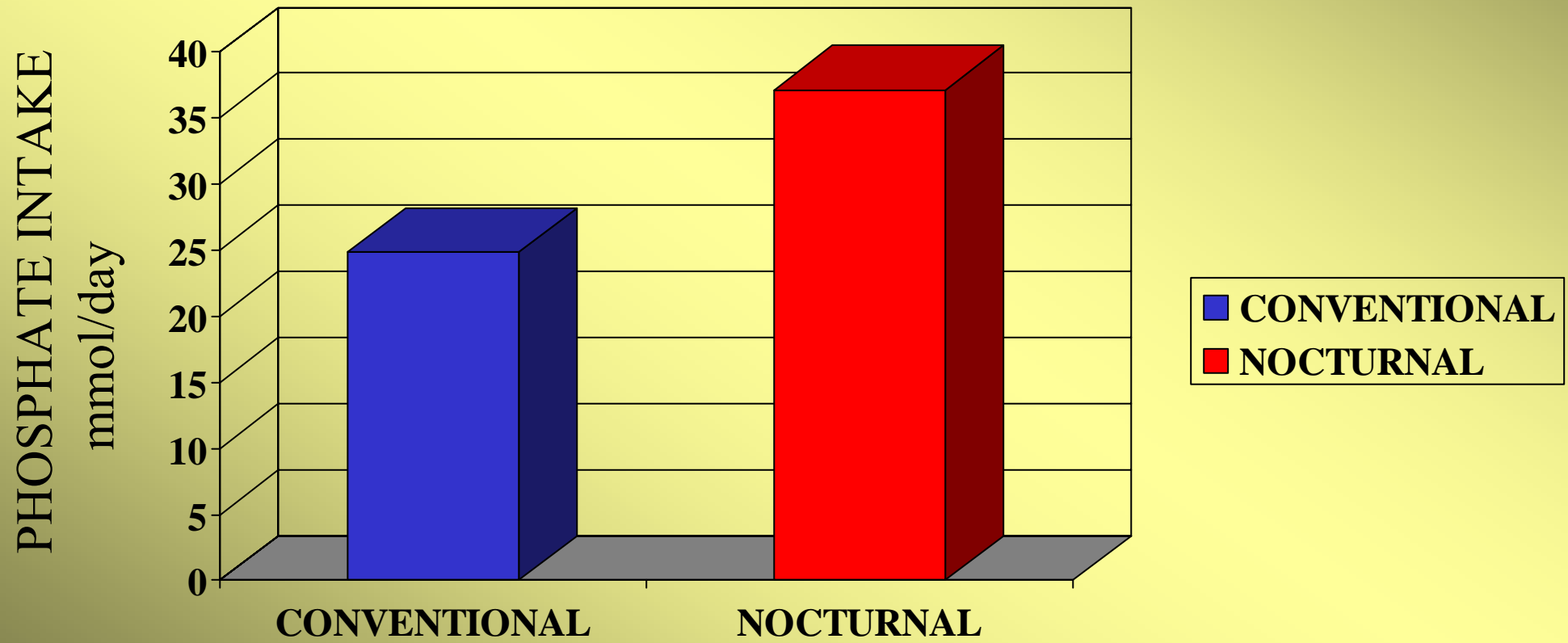
SERUM PHOSPHORUS DURING DIALYSIS



NOCTURNAL HD AND PHOSPHATE CONTROL



DIETARY PHOSPHATE INTAKE: CONVENTIONAL vs NOCTURNAL HD



CONVENTIONAL HD vs NOCTURNAL HD: PHOSPHATE CONTROL

- PHOSPHATE LEVELS
 - 2.1 mmol/L (~6 mg/dL) DECREASED TO 1.3 mmol/L (~3.9 mg/dL) WITH THE START OF NOCTURNAL HD
- BY THE 4th MONTH OF NOCTURNAL HD, ***NONE OF THE PATIENTS WERE USING PHOSPHATE BINDERS***

NOCTURNAL vs DAILY SHORT HEMODIALYSIS

- NOCTURNAL HD
 - LONG TREATMENTS
 - PHOSPHATE CONTROL IMPROVED
 - BLOOD PRESSURE CONTROL IMPROVED
 - ALBUMIN IMPROVED
 - HOME THERAPY
- DAILY SHORT HD
 - SHORT TREATMENTS
 - PHOSPHATE CONTROL NOT IMPROVED
 - BLOOD PRESSURE CONTROL IMPROVED
 - ALBUMIN IMPROVED
 - HOME OR IN-CENTER THERAPY

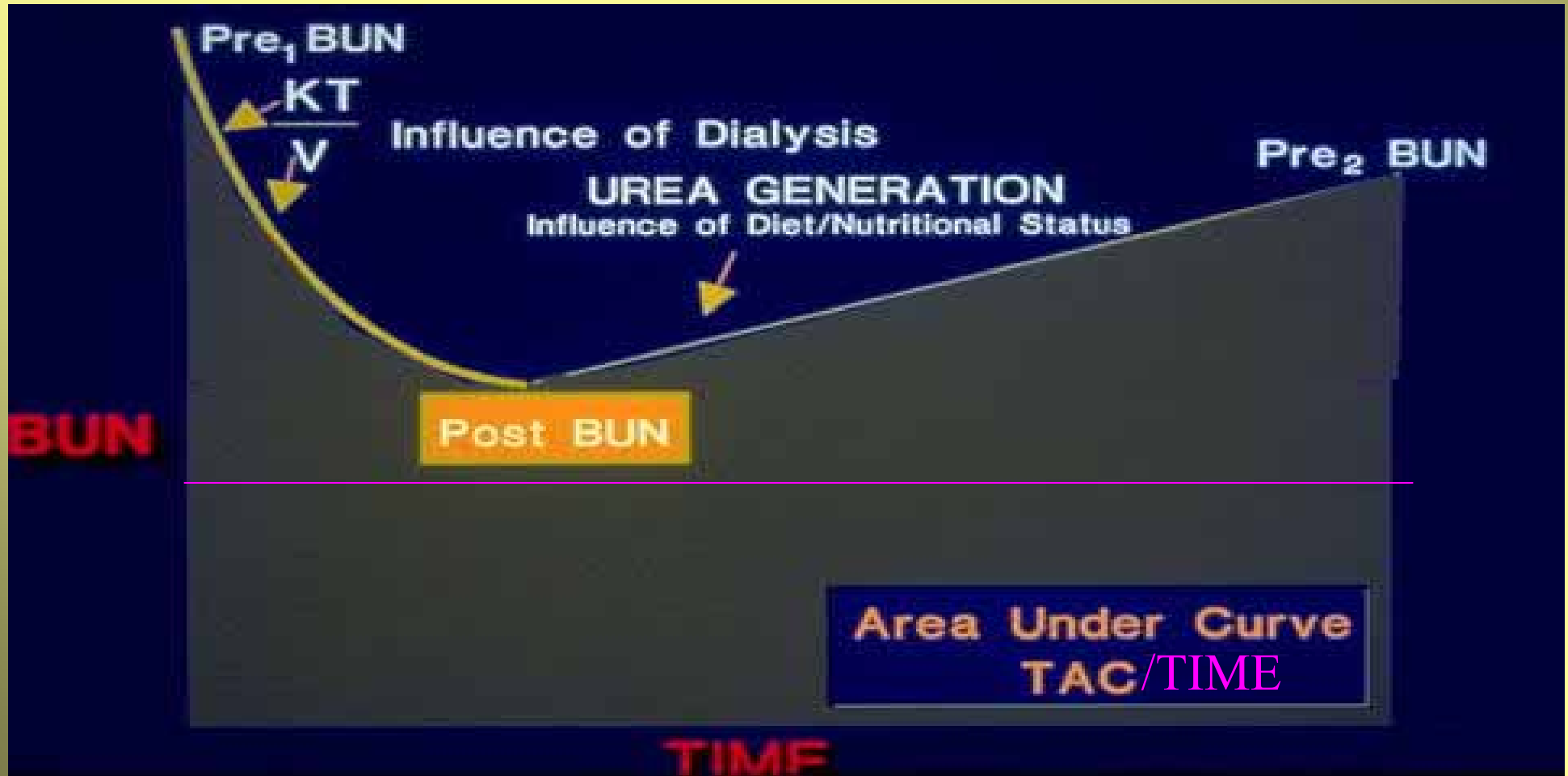
PRINCIPLE BEHIND THE USE OF STANDARD Kt/V

- **UREA IS REMOVED IN A MORE EFFICIENT MANNER AT THE SAME WEEKLY Kt/V AS YOU INCREASE DIALYSIS FREQUENCY.**
- **REMOVAL OF LESS DIFFUSIBLE SOLUTES IS EVEN MORE EFFICIENT AT THE SAME WEEKLY Kt/V .**

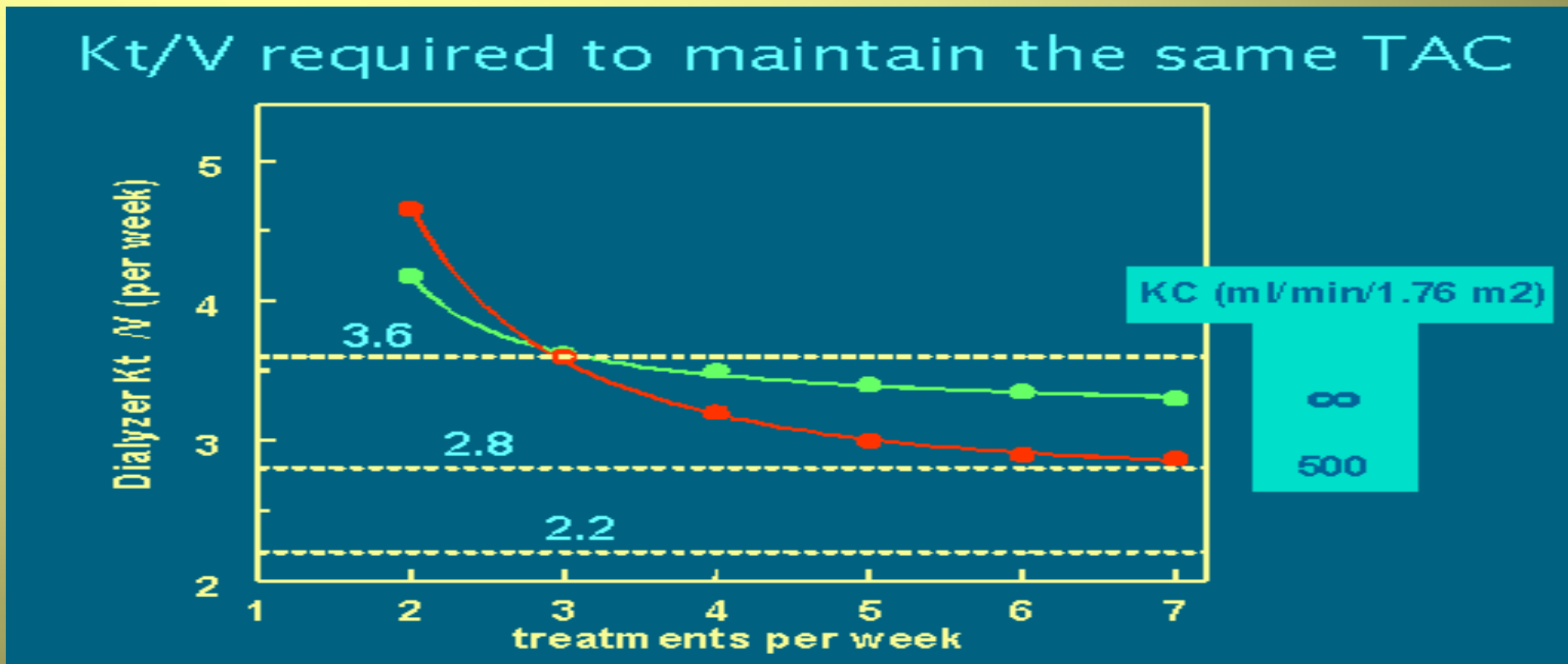
STATUS OF DAILY DIALYSIS

- NO PROSPECTIVE STUDIES OF INCIDENT PATIENTS
- PATIENT SELECTION IS NOT RANDOM
- PATIENTS NUMBER IN THE 100'S
- NO STANDARDIZATION OF REGIMENS
- NO OUTCOME STUDIES
- NOCTURNAL vs DAILY
- ACCESS FUNCTION NOT COMPROMISED

THE DIALYSIS CYCLE



THE EFFECT OF FREQUENCY ON WEEKLY Kt/V



As you increase the frequency, on the x axis here, and maintain the same time average BUN, the need for dialysis diminishes, the dose of dialysis expressed on a weekly basis is less.

RATIONALE FOR USING THE STANDARD K_t/V

- Predicts the currently accepted minimum standard for continuous urea clearance.
- Predicts the approximate level of native kidney urea clearance requiring dialysis intervention.

STANDARD Kt/V

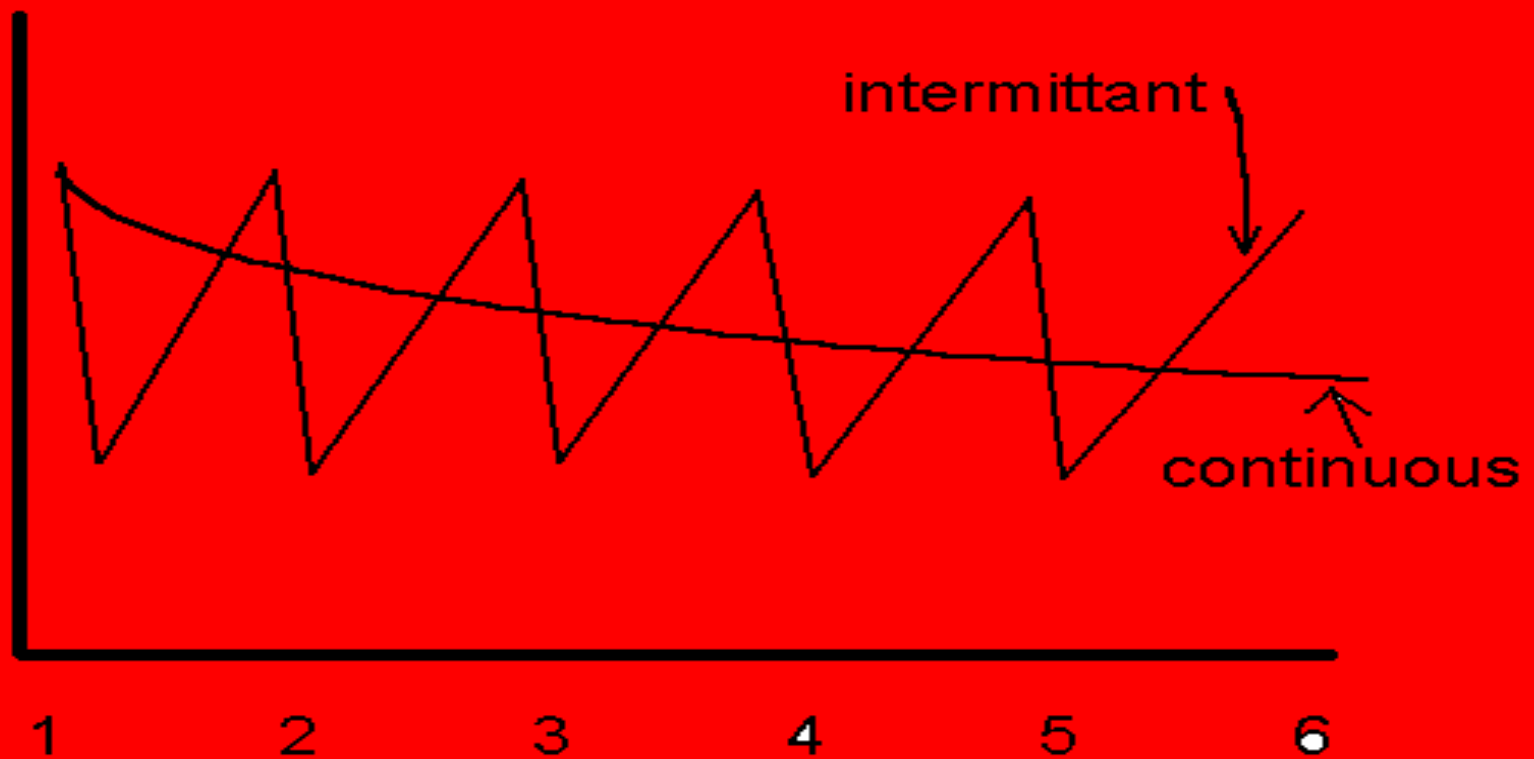
$$\text{Standard } Kt/V = \frac{\text{continuous removal rate}}{\text{average peak concentration}}$$

In a steady state, removal is equal to generation (G).

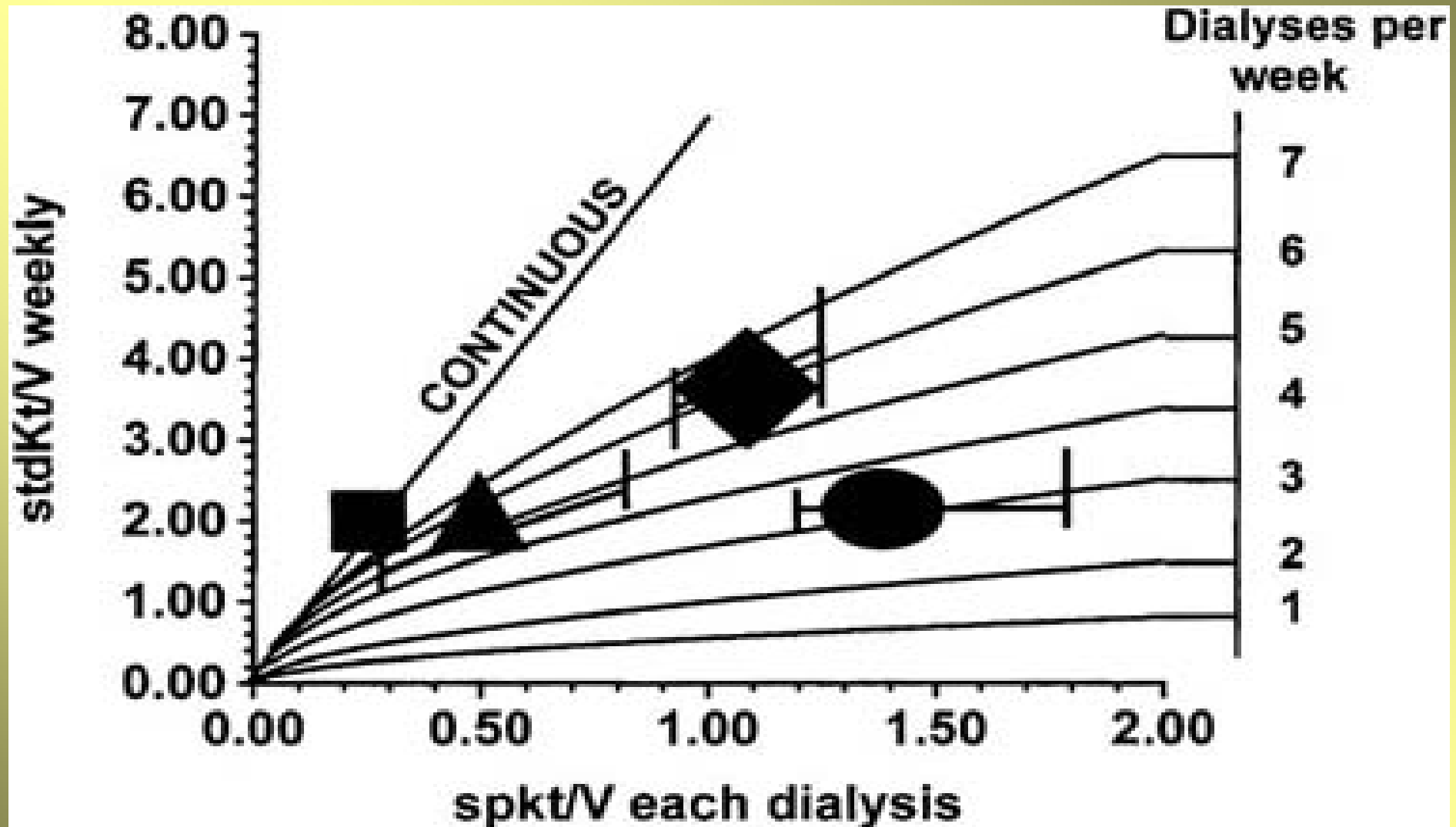
$$\text{Standard } Kt/V = \frac{G}{\text{average peak concentration}}$$

FOR A CONTINUOUS THERAPY, PEAK=MEAN

CONTINUOUS VS INTERMITTENT THERAPY



STANDARD WEEKLY K_t/V MODEL



■ -CAPD

● -IHD

▲ -SDHD

◆ -NHHD

RELATIONSHIP BETWEEN WEEKLY AND STANDARD K_t/V

MODALITY	WEEKLY K_t/V	STANDARD K_t/V
SHORT DAILY DIALYSIS	3.5-4.5	2.7-3.2
NOCTURNAL HEMODIALYSIS	5.0-6.0	3.7-4.2

SUMMARY AND CONCLUSIONS

- MULTIPLE LINES OF EVIDENCE SUGGEST DAILY TREATMENTS IMPROVE:
 - ADEQUACY
 - BLOOD PRESSURE CONTROL
 - HOSPITALIZATION RATE
 - NUTRITION
- TRIALS OF THE MODALITIES ARE REQUIRED
- NOCTURNAL HD NEEDS TO BE INCLUDED IN SUCH TRIALS
 - LACSON AND DIAZ BUXO:NHD FIRST, DHD SUBSEQUENTLY *AM J KIDNEY DISEASE* 2001; 38:225-230

FREQUENT HEMODIALYSIS STUDY

- 250-300 ESRD PATIENTS RANDOMIZED
 - 12 MONTHS
- PRIMARY OUTCOMES
 - SF-36 PHYSICAL HEALTH COMPOSITE
 - Δ LEFT VENTRICULAR MASS BY MRI
- SECONDARY OUTCOMES
 - DEPRESSION
 - NUTRITION
 - COGNITIVE FUNCTION
 - HYPERTENSION
 - RENAL OSTEOPOSYTOSIS

CONVENTIONAL VS SHORT DAILY HEMODIALYSIS

I) CONVENTIONAL HEMODIALYSIS OF 3 SESSIONS PER WEEK. SUBJECTS MAY REMAIN ON THEIR USUAL DIALYSIS PRESCRIPTION SUBJECT TO A MINIMUM EKT/V OF 1.1 PER SESSION AND A MINIMUM TREATMENT TIME OF > 2.5 HOURS PER SESSION;

II) DAILY HEMODIALYSIS OF 6 SESSIONS PER WEEK, TO MAINTAIN A TARGET EKT/(V_N)* OF 0.90 PER SESSION, AND A TREATMENT TIME OF 1.5 HOURS TO 2.75 HOURS

$$V_N = 3.271V^{2/3}$$

Summary of the Dose Treatment Regimens

Parameter	Conventional HD Regimen	Daily HD Regimen	% Difference in medians; Daily HD vs. Conventional HD
Sessions per week	3	6	100%
Target prescription	Unspecified: subject to a minimum eKt/V of 1.10	$eKt/(V_n) = 0.90$	-
Hours per session	≥ 2.5 (median = 3.50)	1.50 to 2.75 (median = 2.36)	-33%
Maximum interdialytic interval during treatment week (median, hours)	68.5	45.6	-33%
Average interdialytic interval during treatment week (median, hours)	52.5	25.6	-51%
Hours per week (median, 5 th – 95 th percentile)	10.5 (9.0 – 13.1)	14.2 (11.5 – 16.5)	+35%
eKt/V urea per treatment (median, 5 th – 95 th percentile)	1.39 (1.12 – 1.75)	0.92 (0.74 – 1.05)	-34%
Weekly stdKt/V urea (median, 5 th – 95 th percentile)	2.46 (2.16 – 2.80)	3.82 (3.32 – 4.17)	+55%
Weekly eKR β_2 -microglobulin (ml/min/35 L) (median, 5 th – 95 th percentile)	12.8 (10.7 – 15.2)	17.6 (14.6 – 19.8)	+38%
Standardized phosphorus removal (mg/day) (median, 5 th – 95 th percentile)	299 (254-374)	415 (338 – 497)	+39%

Achieved eKt/V for different V's when eKt/(V_n) = 0.90

Patient Weight (kg) (assuming weight = V/0.6)	Patient V (L)	eKt/(V_n)	eKt/V
42	25	0.90	1.01
50	30	0.90	0.95
58	35	0.90	0.90
67	40	0.90	0.86
75	45	0.90	0.83
83	50	0.90	0.80

Relationship of treatment time, eKt/V, and eKt/(V_n) to patient volume (V)*

Patient V (L)	Treatment Time (min)	eKt/V	eKt/(V_n)
< 27.5	189	1.51	1.35
27.5 – 32.5	202	1.43	1.36
32.5 – 37.5	212	1.35	1.34
37.5 – 42.5	224	1.29	1.35
> 42.5	240	1.21	1.34

*N=3285 from RRI database

$$V_N = 3.271V^{2/3}$$

SUMMARY AND CONCLUSIONS

- MULTIPLE LINES OF EVIDENCE SUGGEST DAILY TREATMENTS IMPROVE:
 - ADEQUACY
 - BLOOD PRESSURE CONTROL
 - HOSPITALIZATION RATE
 - **NUTRITION**
- TRIALS OF THE MODALITIES ARE REQUIRED
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PLACES TO GO NEXT

TIME!!

DAILY/NOCTURNAL TREATMENT REGIMENS

THE REAL KEY TREATMENT VARIABLE

MD x t

COMORBIDITY

AFTER DR. C RONCO

THE EYE OF GOD



STANDARD Kt/V : A CONTINUOUS CLEARANCE EQUIVALENT

