KDIGO Controversies Conference
Novel techniques and innovation in blood purification:
How can we improve clinical outcomes in hemodialysis?
October 14-15, 2011
Paris France

Monitoring the Hemodialysis Dose

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Removal of accumulated small solutes is important

How long will I live if I choose to stop dialysis?

This varies from person to person. People who stop dialysis may live anywhere from one week to several weeks, depending on the amount of kidney function they have left and their overall medical condition.

National Kidney Foundation web site

Art Buchwald

Famous as a syndicated humorist in life, after his death he is more notable for his reputation as the man who beat hospice and the kidney machine.

How long will I live if I choose to stop dialysis?

The median time to death after stopping dialysis in a series of 18 patients reported by Rich was 7 days (0-17 days)

Rich A, Palliative Med 15:513-14, 2001.

The cause of death is uremia

- Principal cause: accumulation of toxic solutes normally excreted by the kidney
- Evidence: dialysis works by removing small solutes.
- Death is not due to anemia, vitamin D deficiency, hyperparathyroidism, fluid overload, accumulation of beta 2-microglobulin, etc, etc.

Minimum urea clearance for Hemodialysis

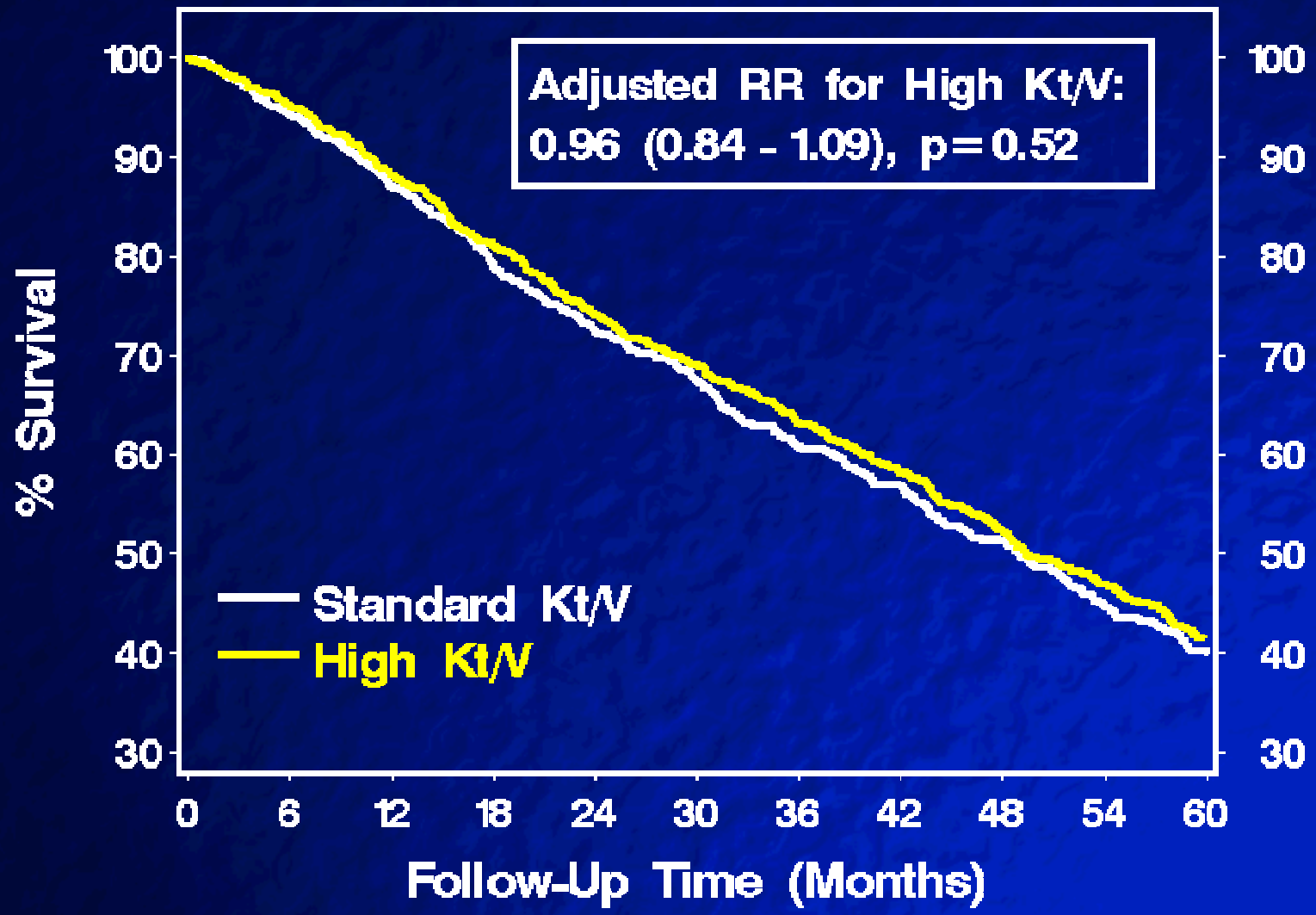
KDOQI guidelines call for a continuous equivalent Kt/V_{urea} of 2.0 volumes/week.

2.0 volumes per week x 35 L = 70 L/week

= 70,000 ml/L /10080 min/week

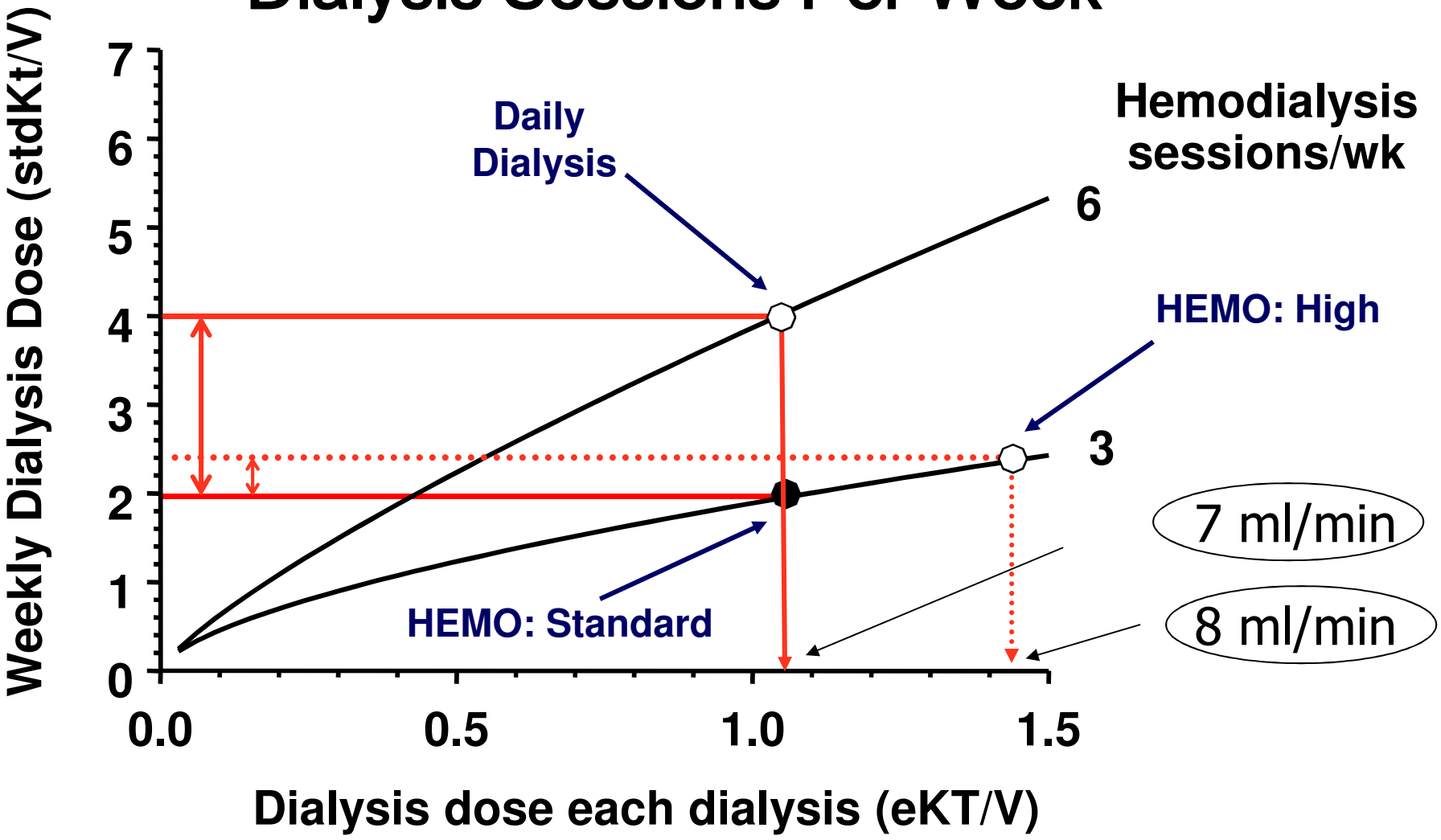
= 7 ml/min

HEMO Study: Survival by Kt/V Group



Eknoyan et al, N Eng J Med 2002

Effect of Increasing Number of Dialysis Sessions Per Week

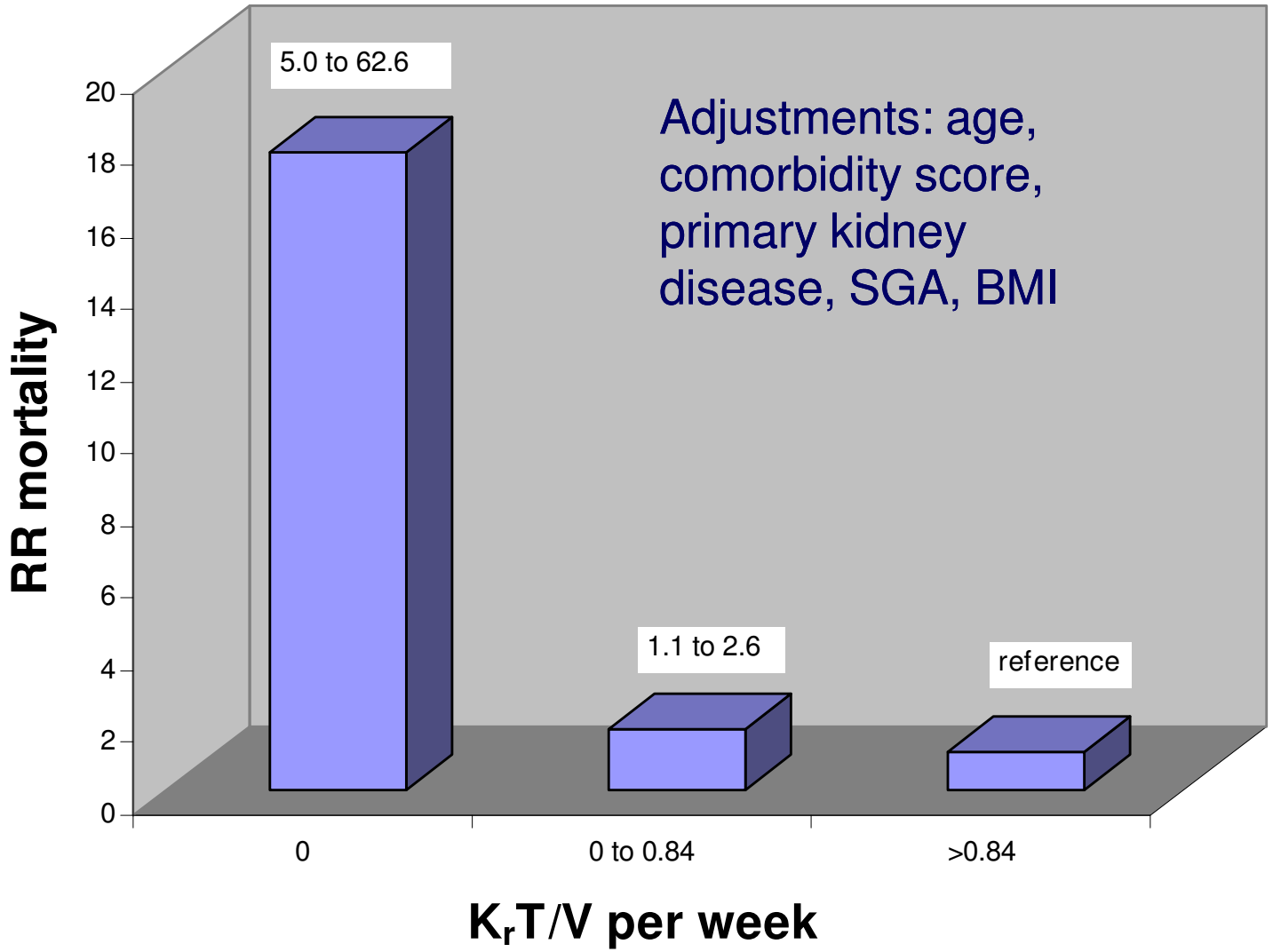


Deficiencies of Kt/V

- Residual kidney function not considered
- Solute disequilibrium is under-represented
- No provision for dialysis frequency
- K and t may not be equivalent
- V is independently associated with outcome
- Non-linear correlation with outcome

Effect of K_r-urea on mortality in HD patients

Termorshuizen F, et al: JASN 15:1061-70, 2004



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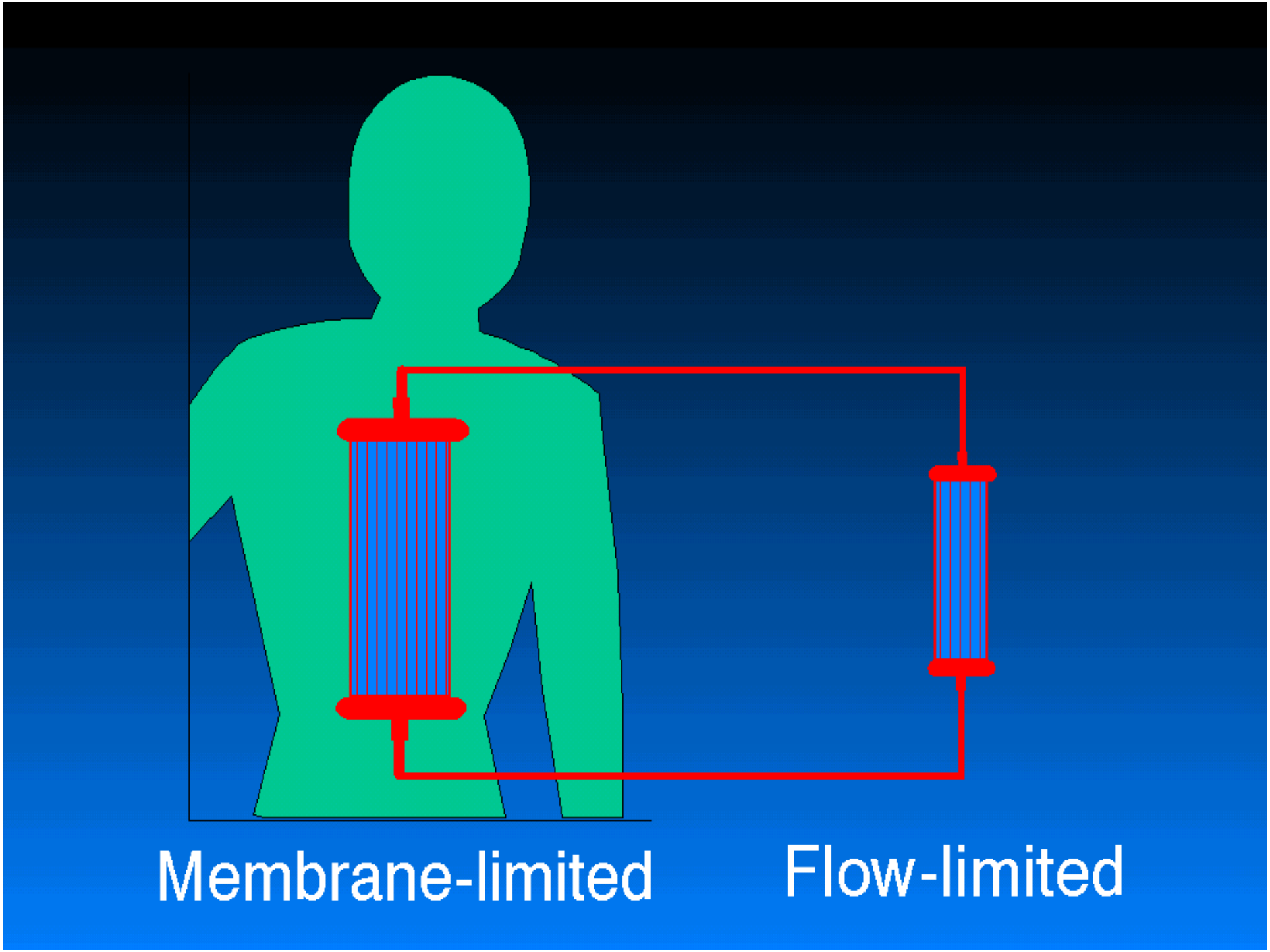
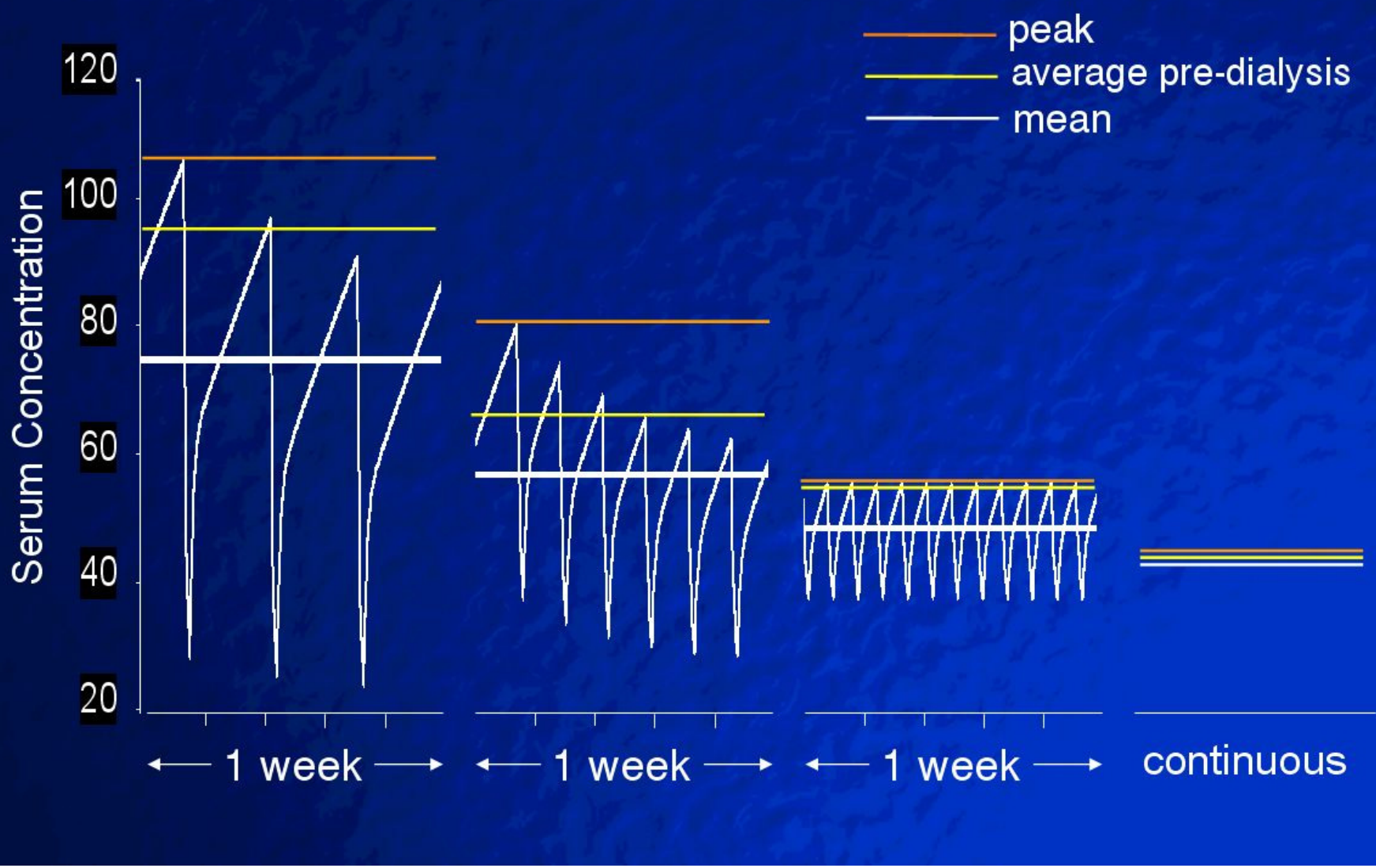

Membrane-limited
Flow-limited

Effect of more frequent dialysis on solute levels

Weekly dialyzer clearance is constant



Standard K (and Kt/V) - Gotch

$$\text{Standard K} = \frac{\text{continuous removal rate}}{\text{average peak concentration}}$$

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

$$\text{Standard K} = \frac{G}{\text{average peak concentration}}$$

Standard Kt/V

$$_{std}Kt/V = \frac{10080\,\dfrac{1-e^{-eKt/V}}{t}}{\dfrac{1-e^{-eKt/V}}{eKt/V} + \dfrac{10080}{Nt} - 1}$$

Gotch, FA: Nephrol Dial Transplant 13 Suppl 6:10-14, 1998

Leypoldt, JK: Seminars In Dialysis 17:142-145, 2004

Standard Kt/V adjusted for Uf and Kru

$$\text{std}Kt/V = S/[1 - (0.74/F) \bullet Uf/V] + Kru \bullet [0.974/(spKt/V + 1.62) + 0.4] \bullet 10/V$$

S is the unadjusted stdKt/V per week

F is the number of dialyses/week

Uf is the weekly fluid removal in liters

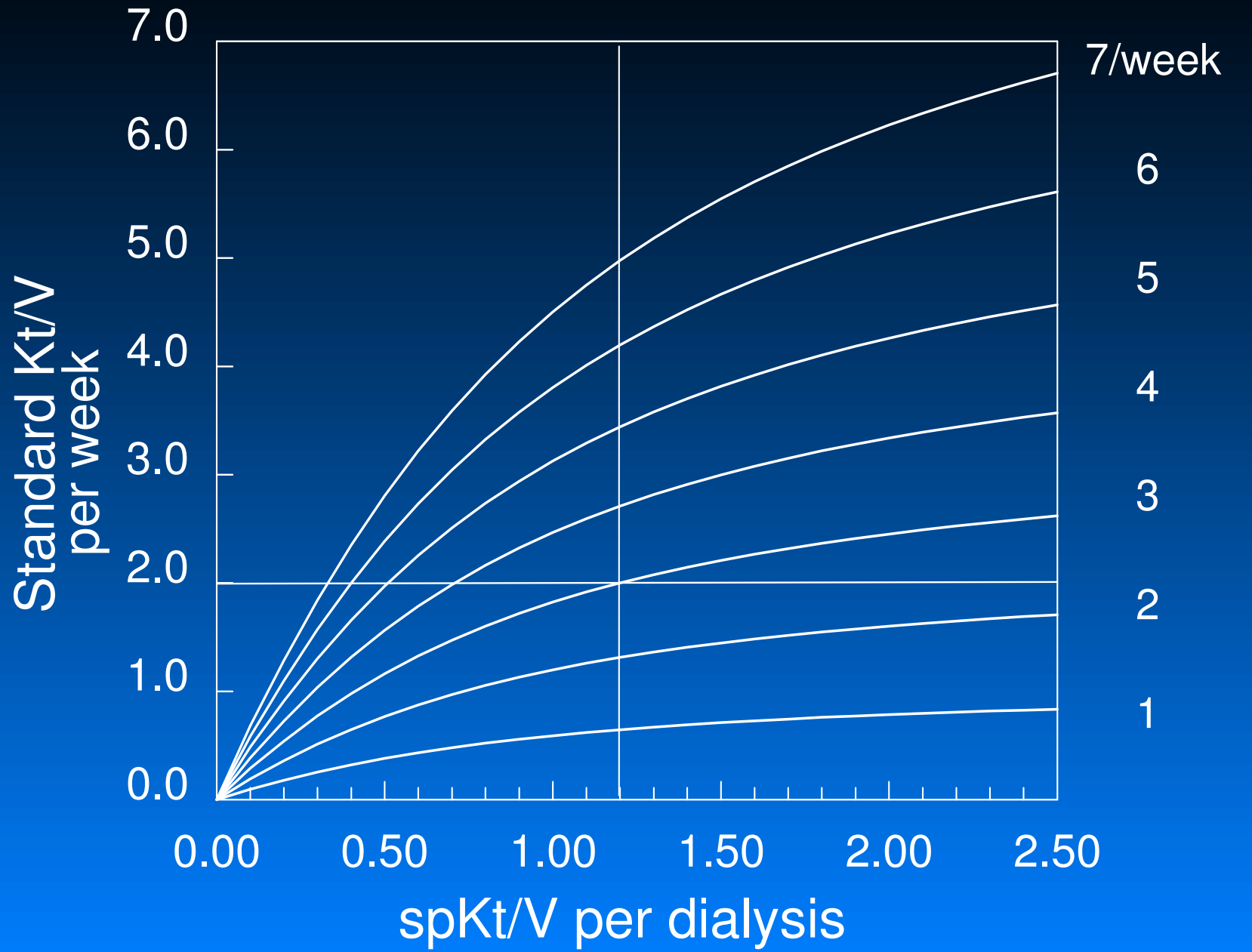
Kru is the residual native kidney clearance of urea in ml/min

spKt/V is the single pool Kt/V per dialysis

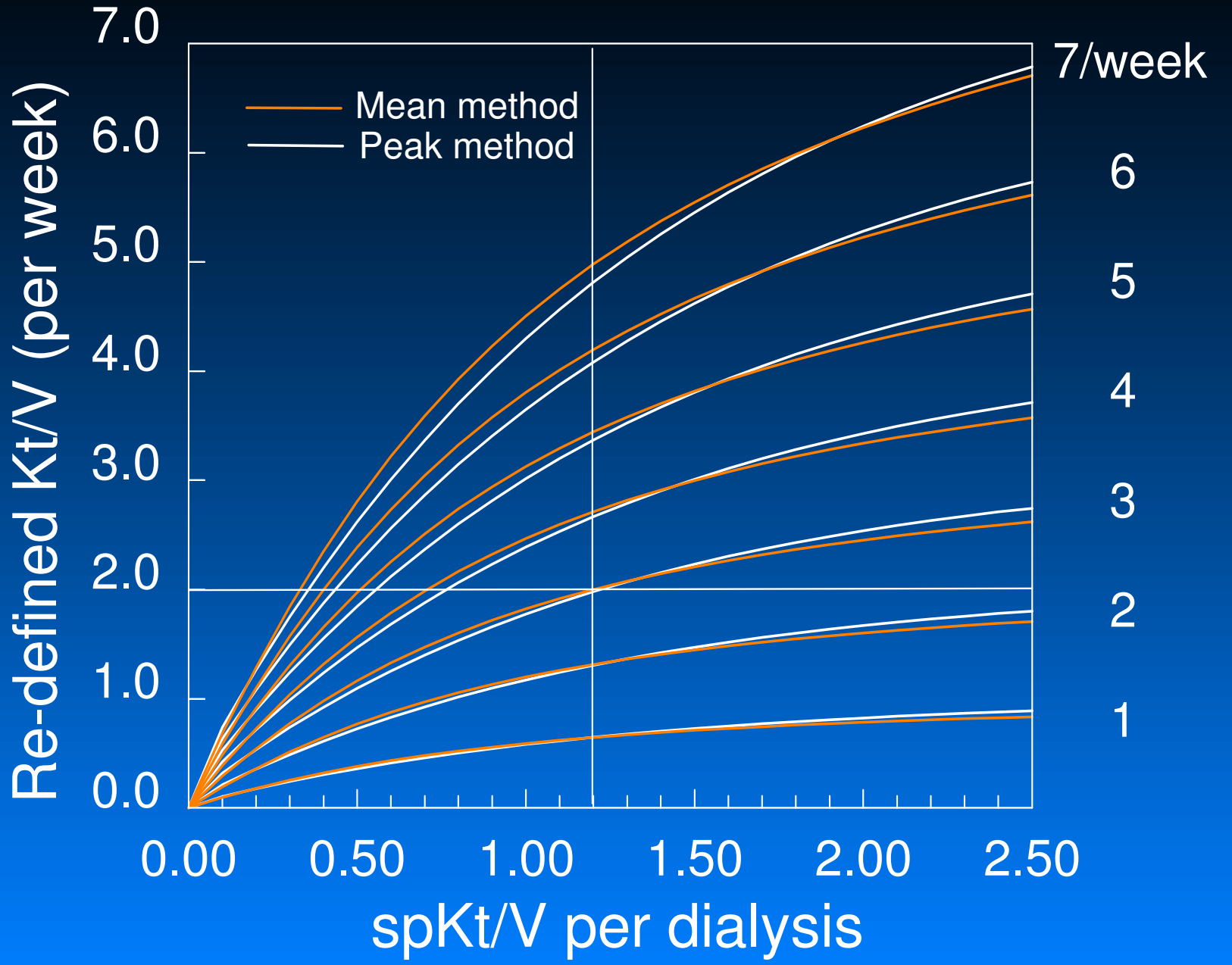
V is the urea distribution volume in liters

Daugirdas J, et al: Kidney Int 2010

Continuous vs. intermittent clearance expressions



Continuous versus peak concentration methods



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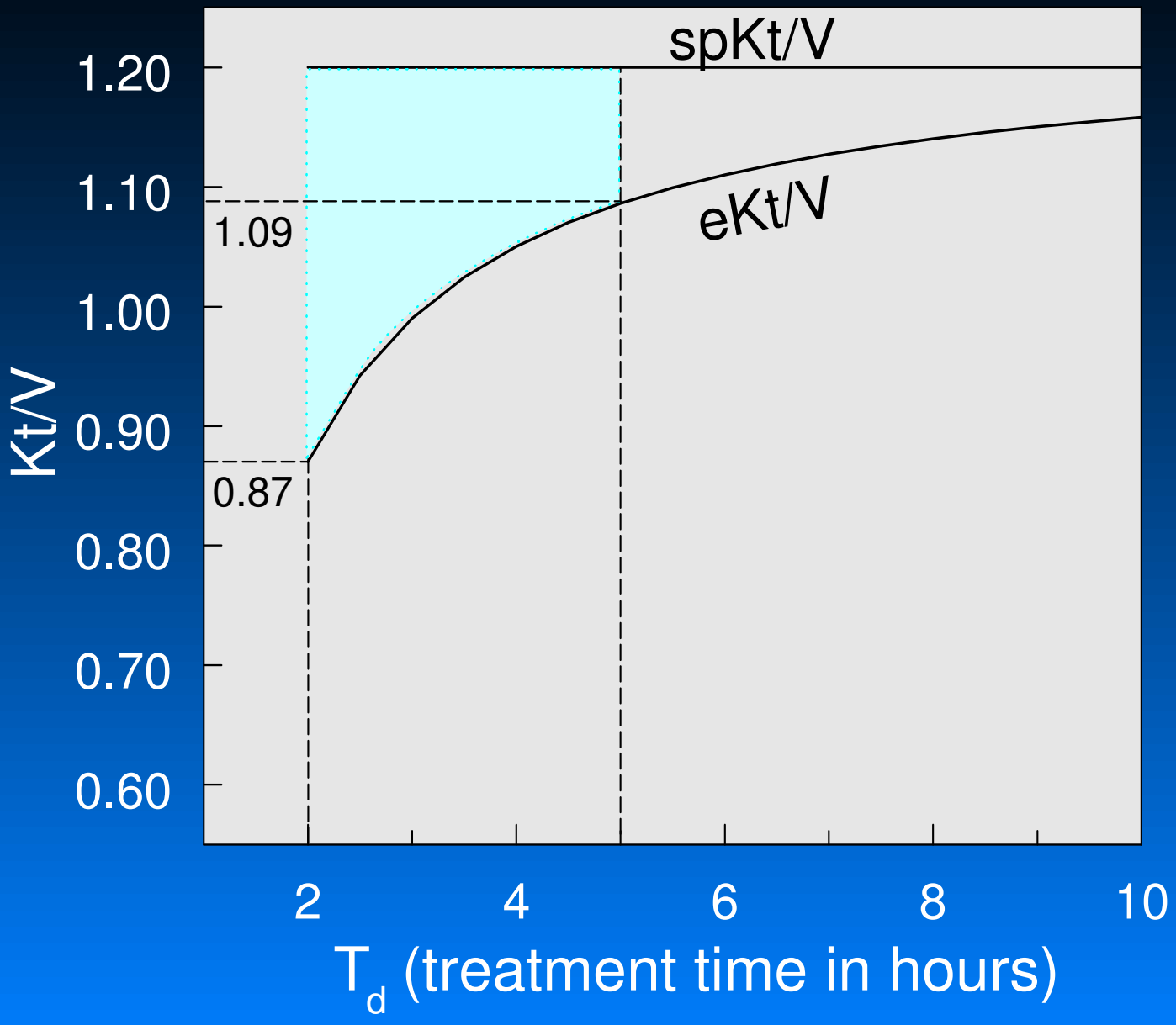
Effect of treatment time on eKt/V



Treatment time predicts mortality

Saran et al from DOPPS, Kid Int 69:1222-28, 2006

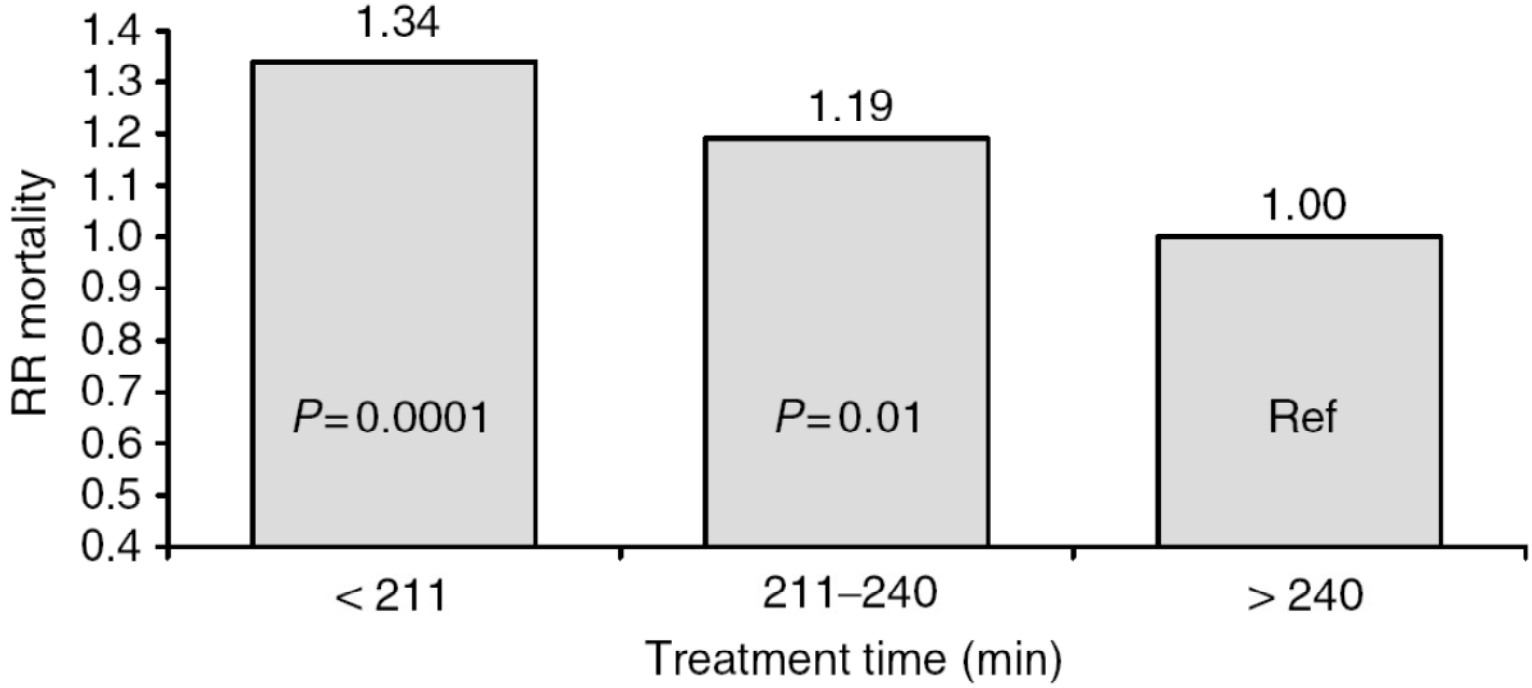


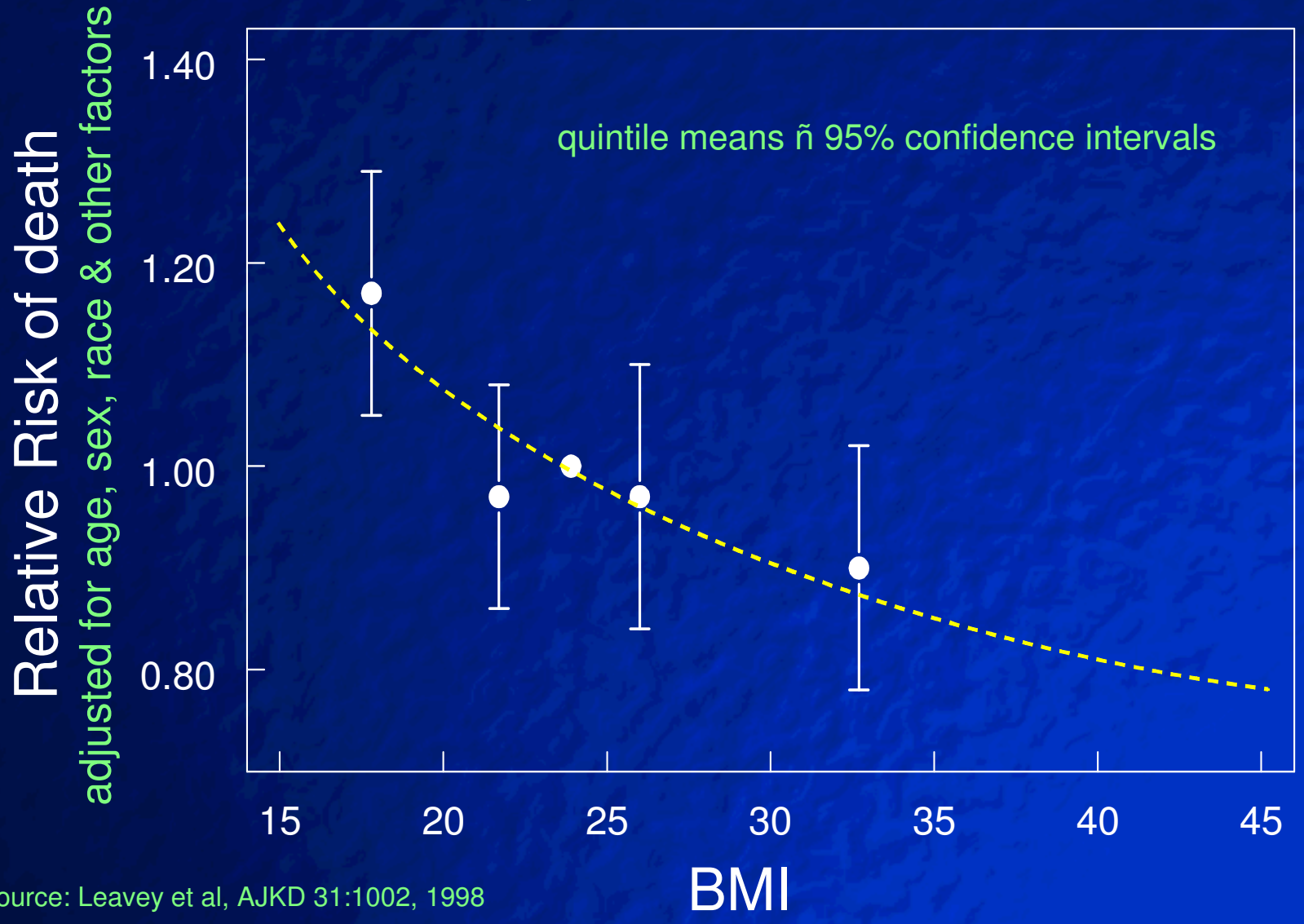
Figure 2 | RR of all-cause mortality, by TT category.
The incremental RR of mortality with decreasing TT categories in all DOPPS regions combined. The referent category is TT > 4 h (240 min).

KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE

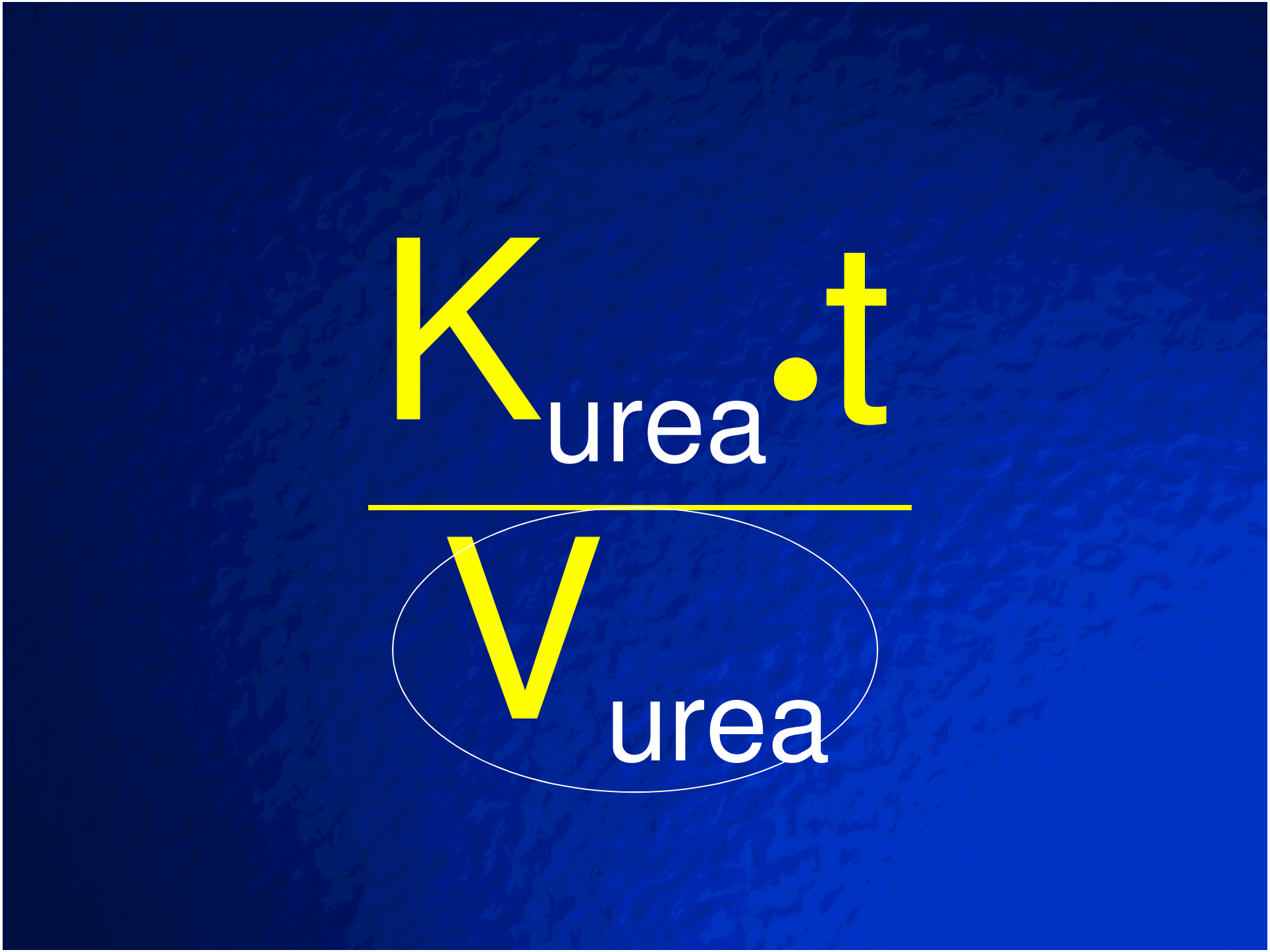
New NKF-KDOQI Hemodialysis Guidelines

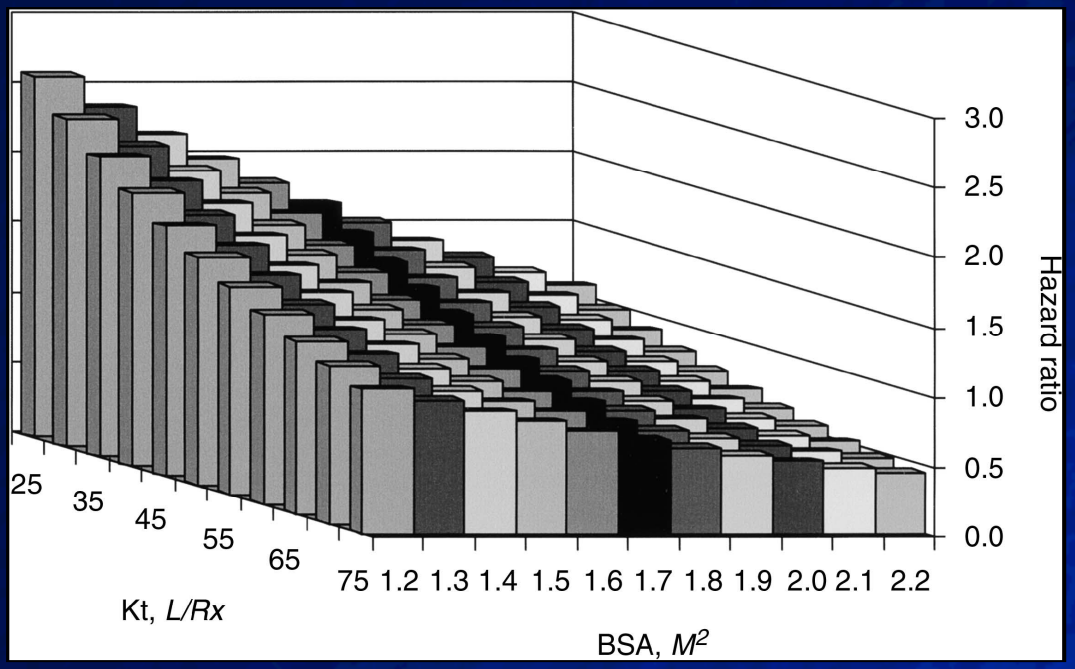
Mortality and Body Mass Index

USRDS: 3607 patients enrolled in CMAS, Jan 1991



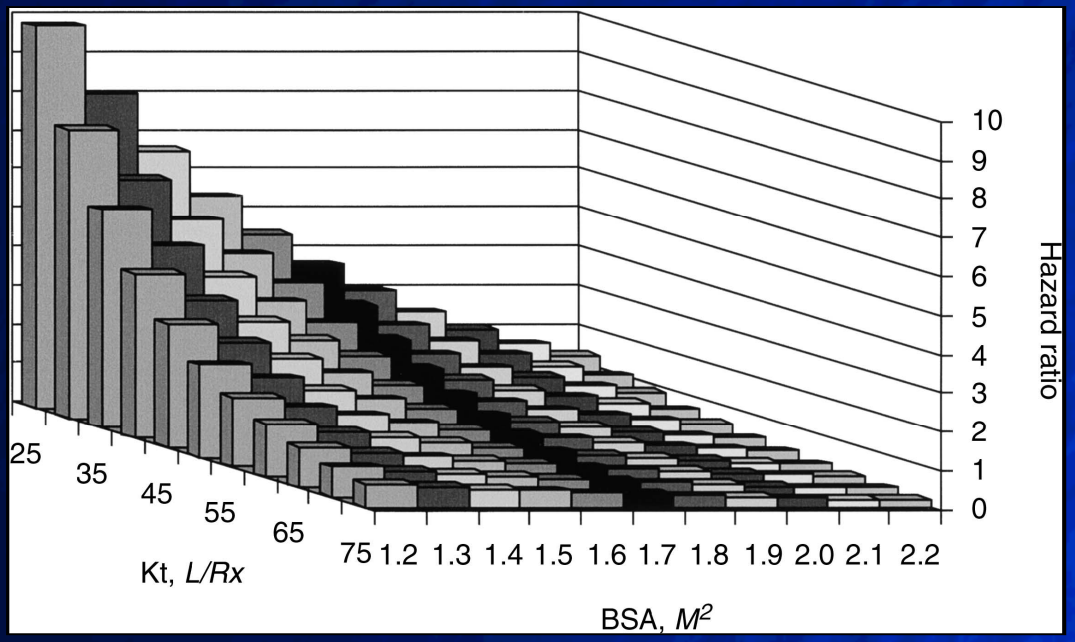
Source: Leavey et al, AJKD 31:1002, 1998


$\frac{K_{urea} \cdot t}{V_{urea}}$



43,334 patients

Continuous risk (hazard) plane for Kt and BSA. The analysis did not include an interaction term between Kt and BSA and was case mix adjusted.



Continuous risk (hazard) plane for Kt and BSA. The analysis included an interaction term between Kt and BMI and was case mix adjusted.

Lowrie E, et al: KI 62:1891-7, 2002

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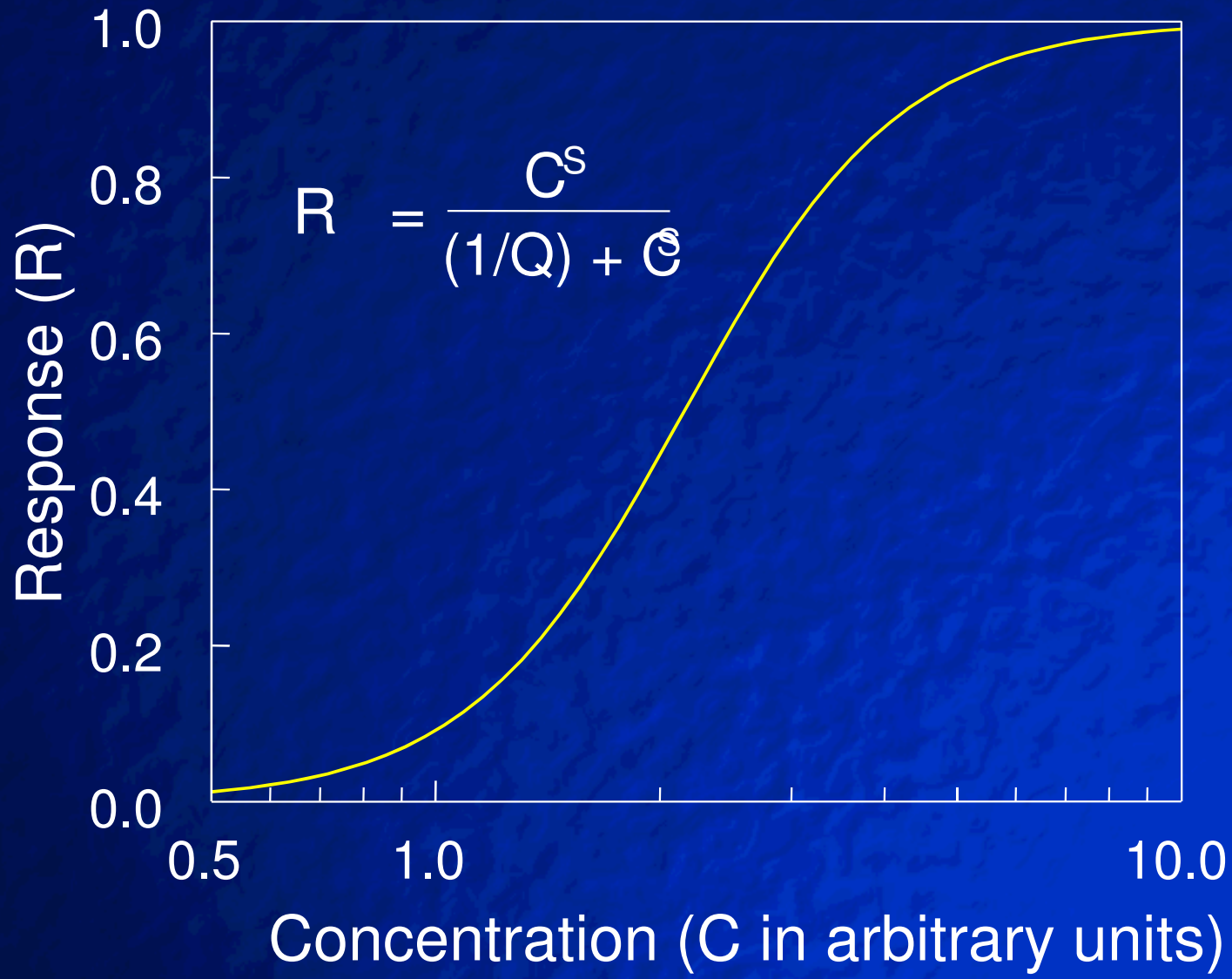
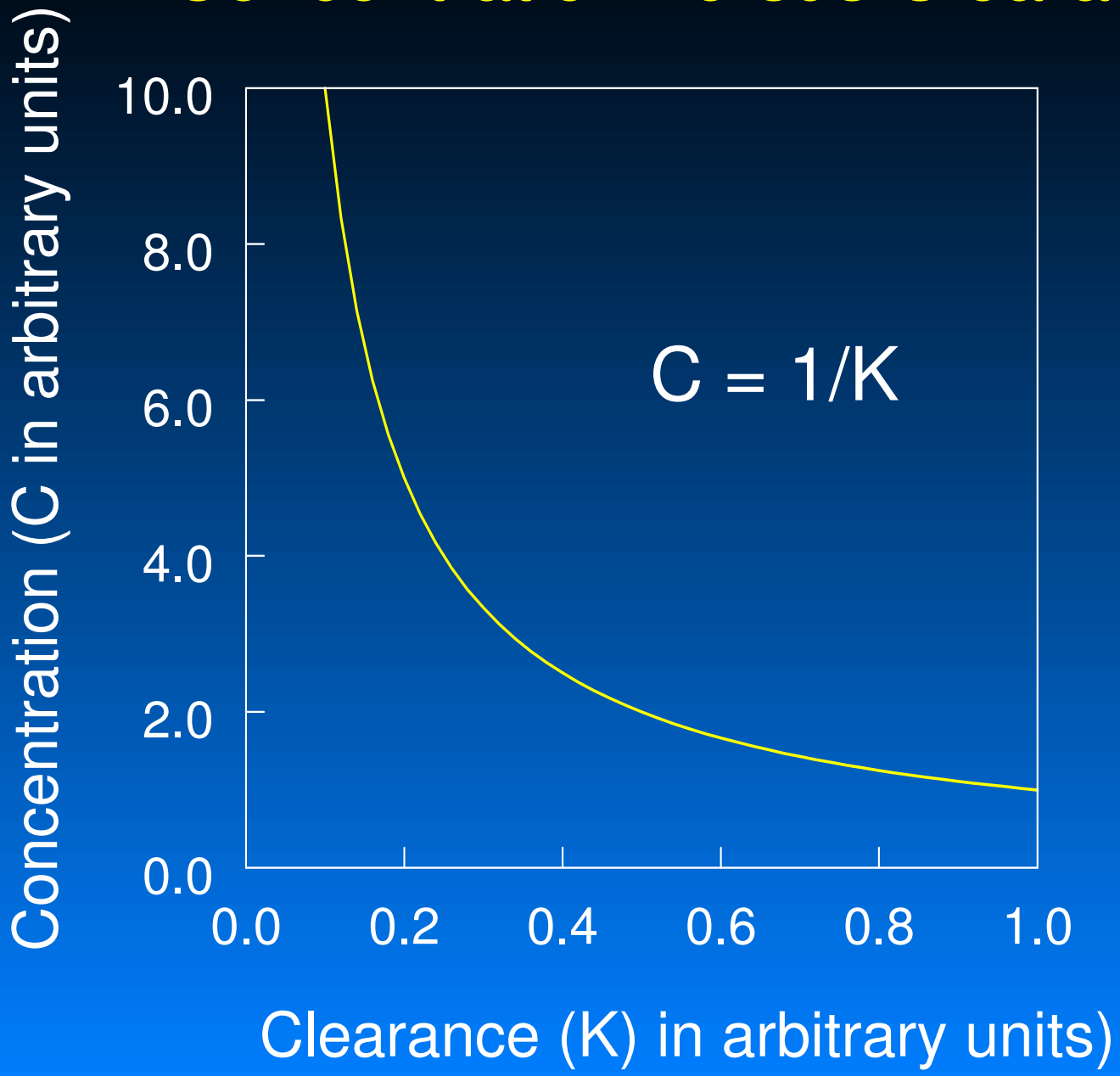
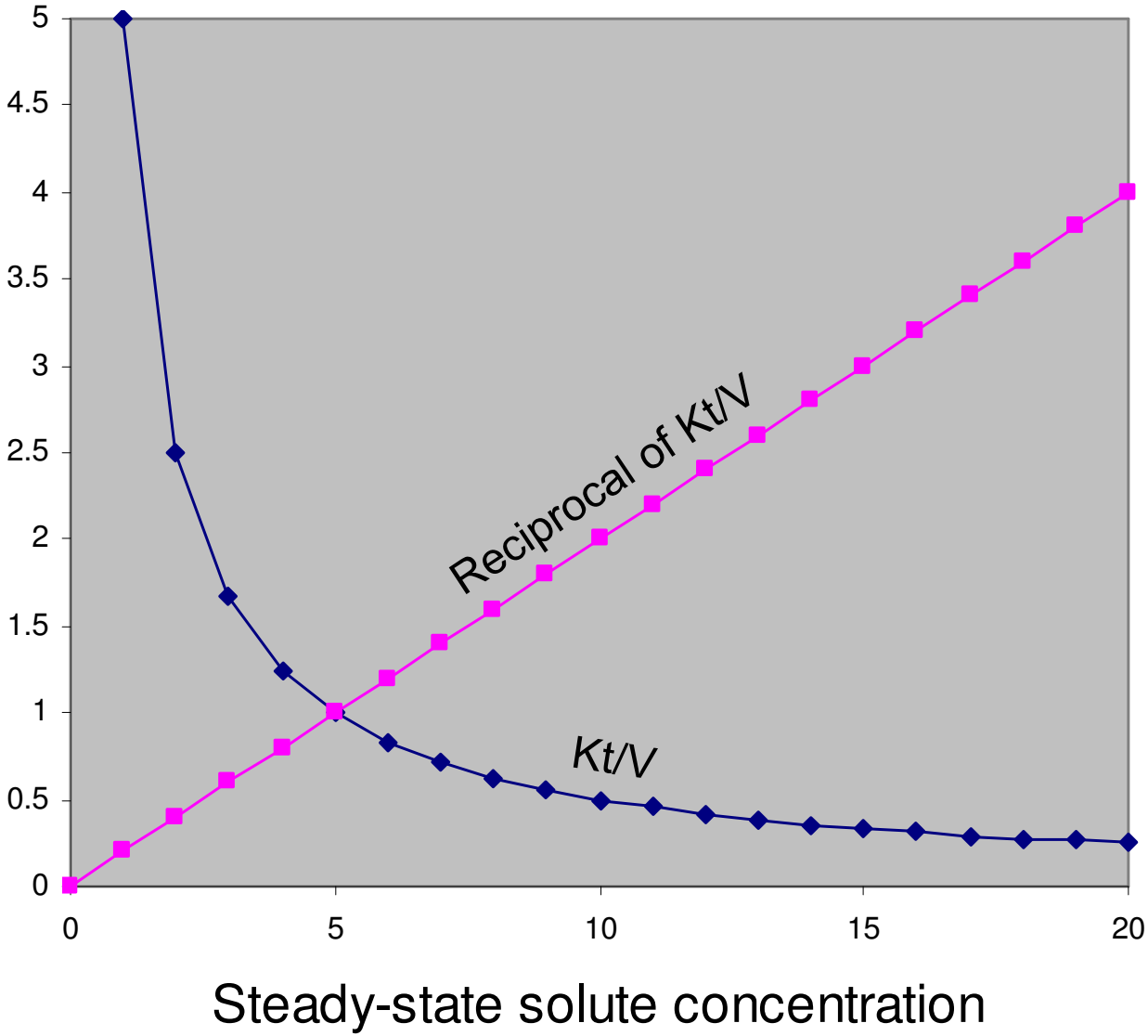
Concentration (Dose) - Response Curve

Hill equation: applies to a direct reversible effect



Concentration versus Clearance




5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
5
10
15
20
Reciprocal of Kt/V
Kt/V
Steady-state solute concentration

Some proposed improvements to Kt/V

- Include residual native kidney clearance (Kr)
- Account for solute disequilibrium
  - » eKt/V
- Allow for more frequent dialysis
  - » Standardized Kt/V
- Index to surface area instead of V
- Tighter correlation with outcome
  - » reciprocal of Kt/V

Summary: uremia is a complex state

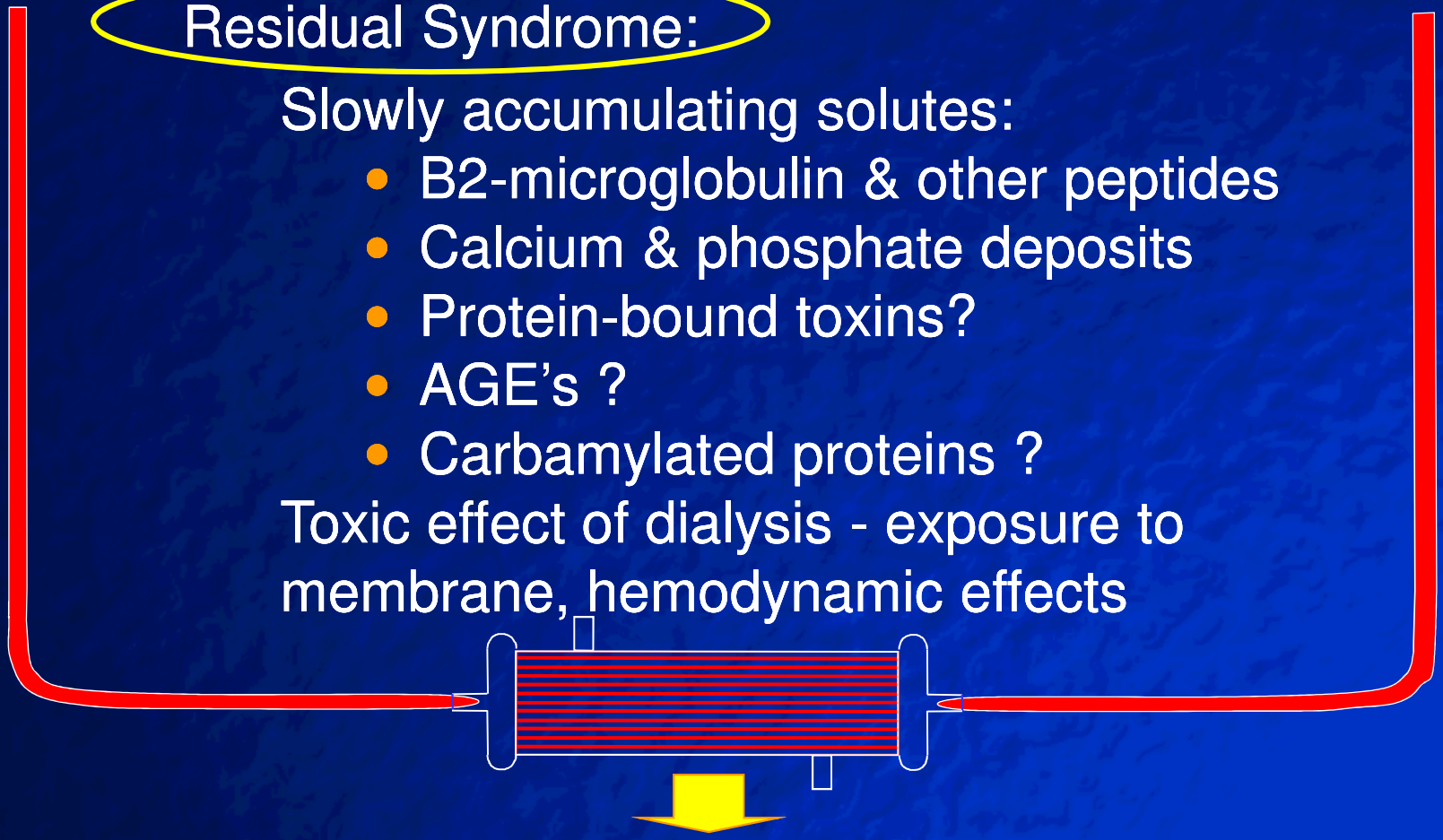
Comorbidity (DM, CVD, nutrition, anemia, etc)

Residual Syndrome:

Slowly accumulating solutes:

- B2-microglobulin & other peptides
- Calcium & phosphate deposits
- Protein-bound toxins?
- AGE's ?
- Carbamylated proteins ?

Toxic effect of dialysis - exposure to membrane, hemodynamic effects



Life threatening toxins

Future of dose monitoring

Because control of small solute concentrations must be the principal goal of replacement therapy, future efforts should focus not on whether we should measure small solute clearance, but what else we should measure and do for our patients.

Adequacy of Dialysis

= Removal of Toxins

= Prevention of Uremia

= Restoration of Health