Hemodialysis adequacy

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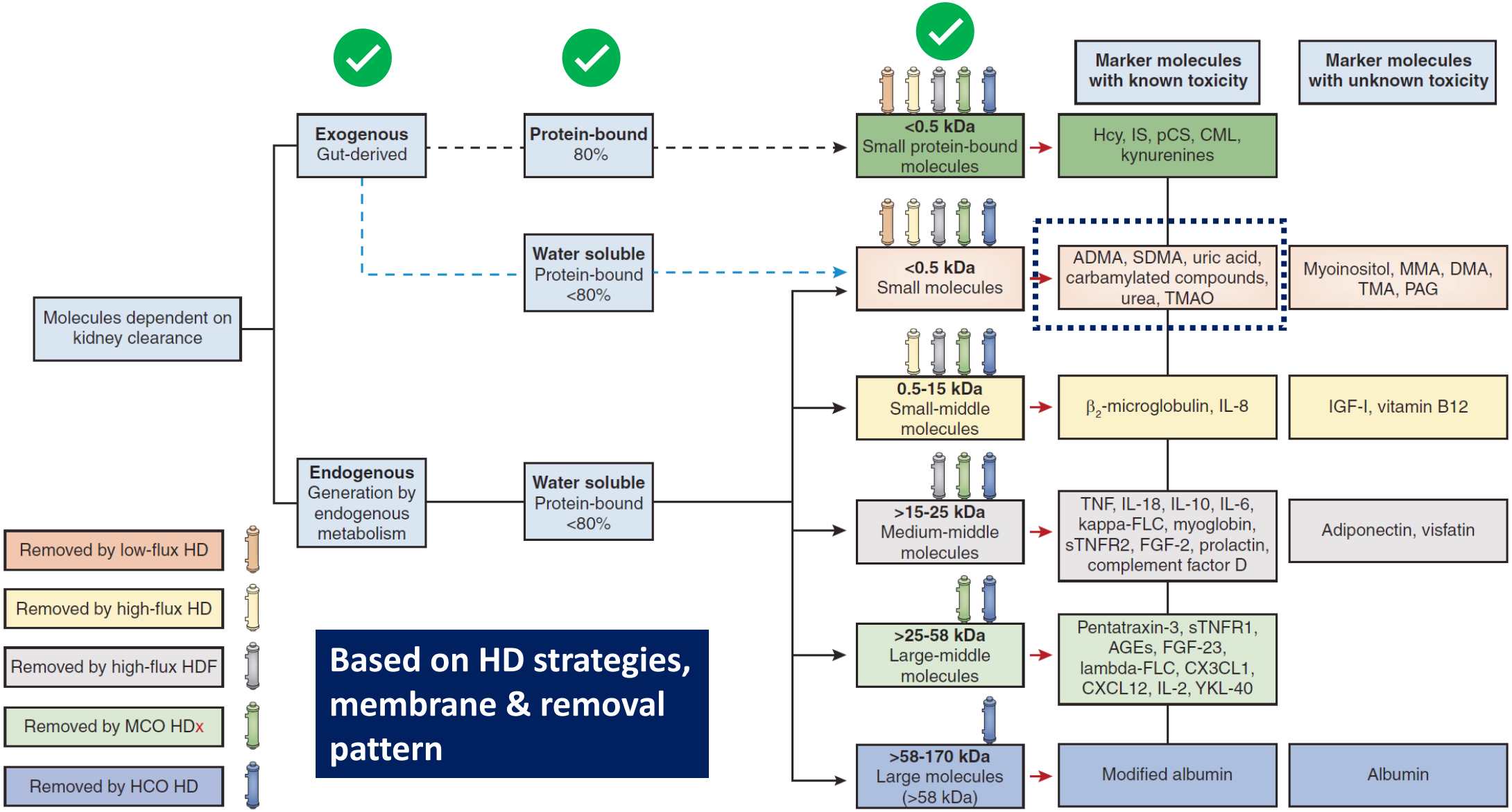
Outline

- Dialysis adequacy: goal?
- Uremic toxin & Urea
- Urea kinetic model
- spKt/V, eKt/V, stdKt/V
- Is minimum spKt/V adequate?
- Approaching Kt/V changes
- Take home message

Uremic toxin: classification



Rosner MH, et al. Clin J Am Soc Nephrol. 2021 Dec;16(12):1918-1928.

Ideal uremic toxin for dialysis goal

- Proven toxicities in human
- Elevated in CKD > healthy; need kidney clearance
- Cleared by dialysis (i.e. diffusion): small molecule & freely filtered
- Correlates with another similar uremic toxins
- Widely available test
- Evidence-based (proven for improved outcomes if removed adequately, e.g. better survival)

Brenner and Rector's the Kidney, 11th edition.
Rosner MH, et al. Clin J Am Soc Nephrol. 2021 Dec;16(12):1918-1928.

Urea: ideal uremic toxin?

Urea: a **small**-60-Da molecule, freely distributed (mostly) between compartments, waste product of **amino-acid** metabolism produced by **liver** & cleared by kidney

- **Proven toxicities in human** ?
- **Elevated in CKD > healthy** ✓
- **Cleared by dialysis** ✓
- **Correlates with another similar uremic toxins** ?
- **Widely available test** ✓
- **Evidence-based, yes but strong…** ?

Vanholder R, et al. Kidney Int. 2015 Sep;88(3):460-5.
Rosner MH, et al. Clin J Am Soc Nephrol. 2021 Dec;16(12):1918-1928.

NCDS & re-analysis

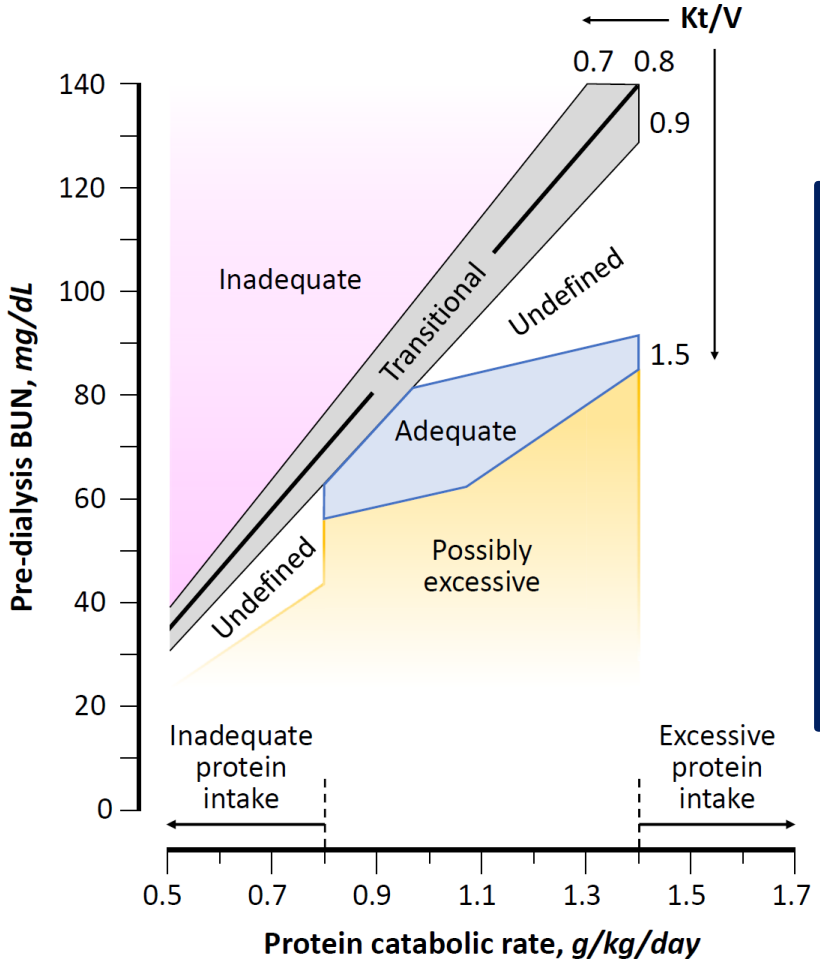
HD patients age 18-70 y, **protein intake 0.8-1.4 g/kg/d**
RKF < 3 mL/min, Cellulose membrane

Session length/TAC	TAC* 50 mg/dL (pre-dialysis 70 mg/dL)	TAC 100 mg/dL (pre-dialysis 120 mg/dL)
Session length 4 h	Group 1	Group 2
Session length 3 h	Group 3	Group 4

*Time average concentration of Urea

Morbidity = Withdrawn from study (medical reason) or hospitalization
Lower in *group 1, 3* significantly from group 2, 4
TAC_{urea} = significant impact on morbidity
Session length = no significant impact on morbidity

However, TAC_{urea} is dependent on PCR (nutrition)



Re-analysis from NCDS data
Kt/V < 0.8 or PCR < 0.8 g/kg/d is associated with ↑morbidity (57%)
Those with ↓ morbidity (13%) = **matched PCR** ≈ 1 g/kg/d **& Kt/V** ≈ 1 (> 0.9)

If Low PCR, morbidity ↑ by itself
If adequate PCR, *inadequate dialysis* drives morbidity

Gotch FA, Sargent JA. Kidney Int. 1985 Sep;28(3):526-34.
Lowrie EG, et al. N Engl J Med. 1981 Nov 12;305(20):1176-81.

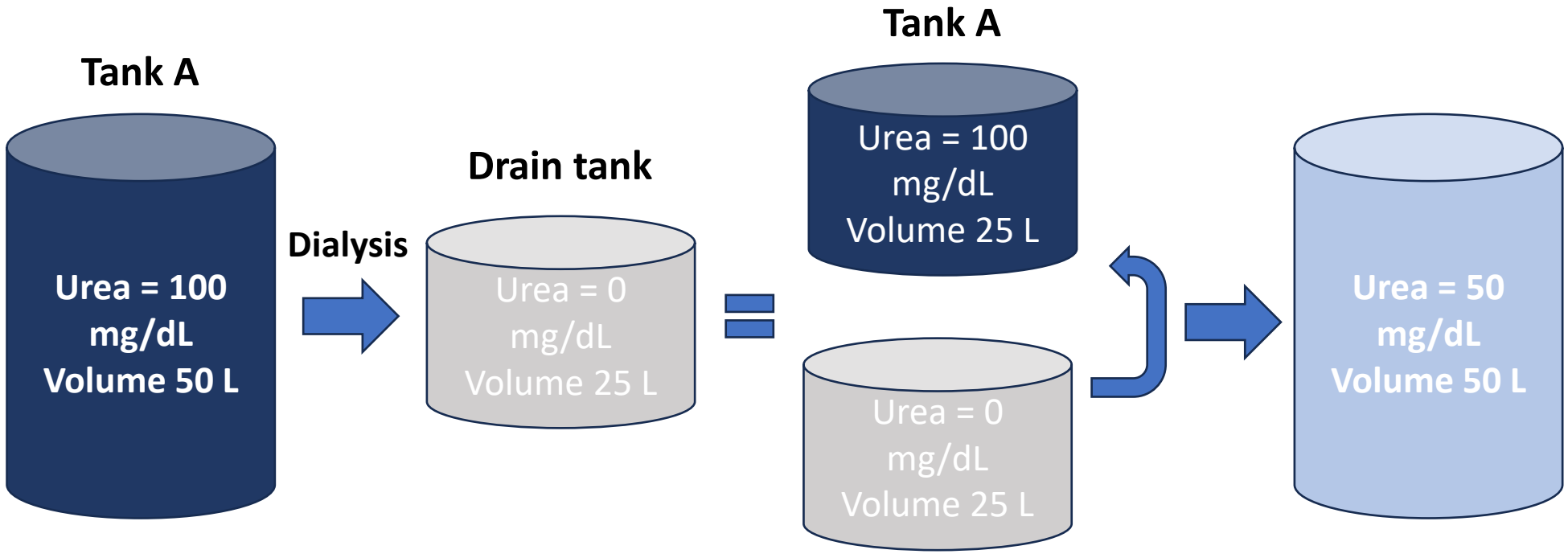
Urea reduction ratio (URR)

Open loop system

$$URR\% = \frac{C_0 - C}{C_0} \times 100$$

C_0 = Pre-dialysis Urea

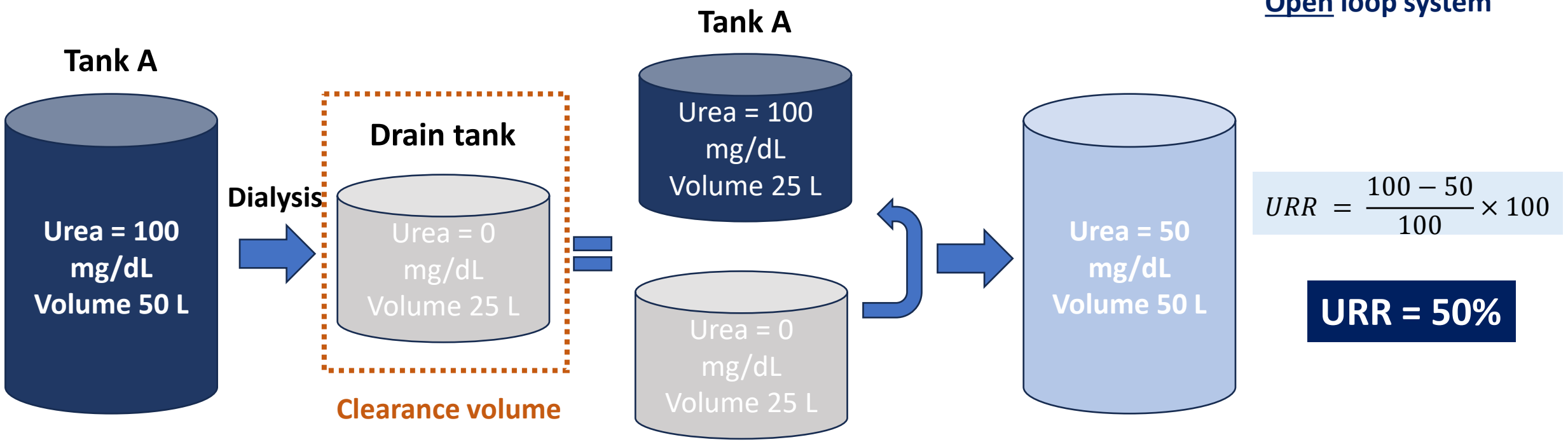
C = Post-dialysis Urea



$$URR = \frac{100 - 50}{100} \times 100$$

URR = 50%

Urea reduction ratio α Kt/V



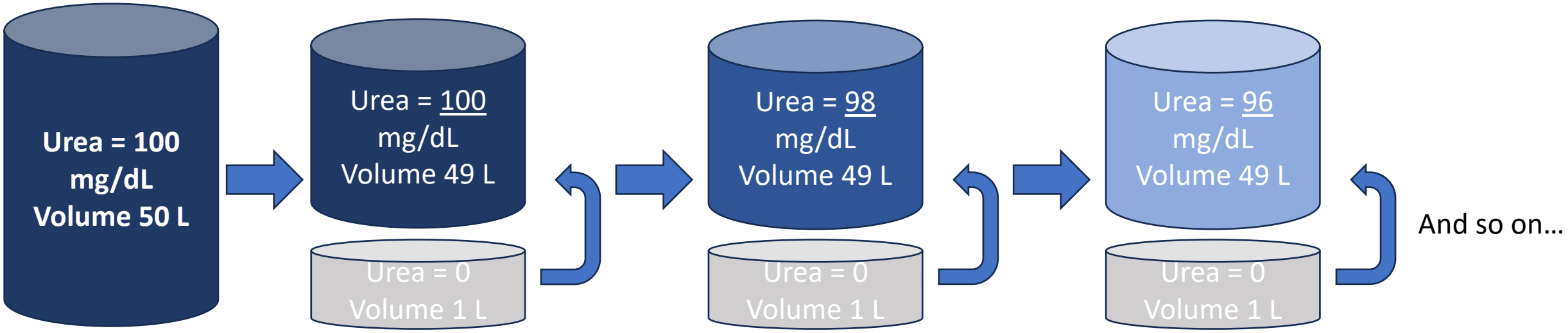
K = Clearance (L/h)
T = time (h)
Kt = Total clearance volume (L)
V = Total Tank volume (L)

Kt/V $= \frac{25}{50} = 0.5 = \boldsymbol{URR}$

Then, why don't we use URR?

URR is not accurate

Closed loop system



If this continue for 50 times (K = 1 L/time; t = 50), cleared volume (Kt) = 50 L, V = 50 L $\left(\frac{K}{V} = \frac{1}{50}\right)$

So, Kt/V = 1

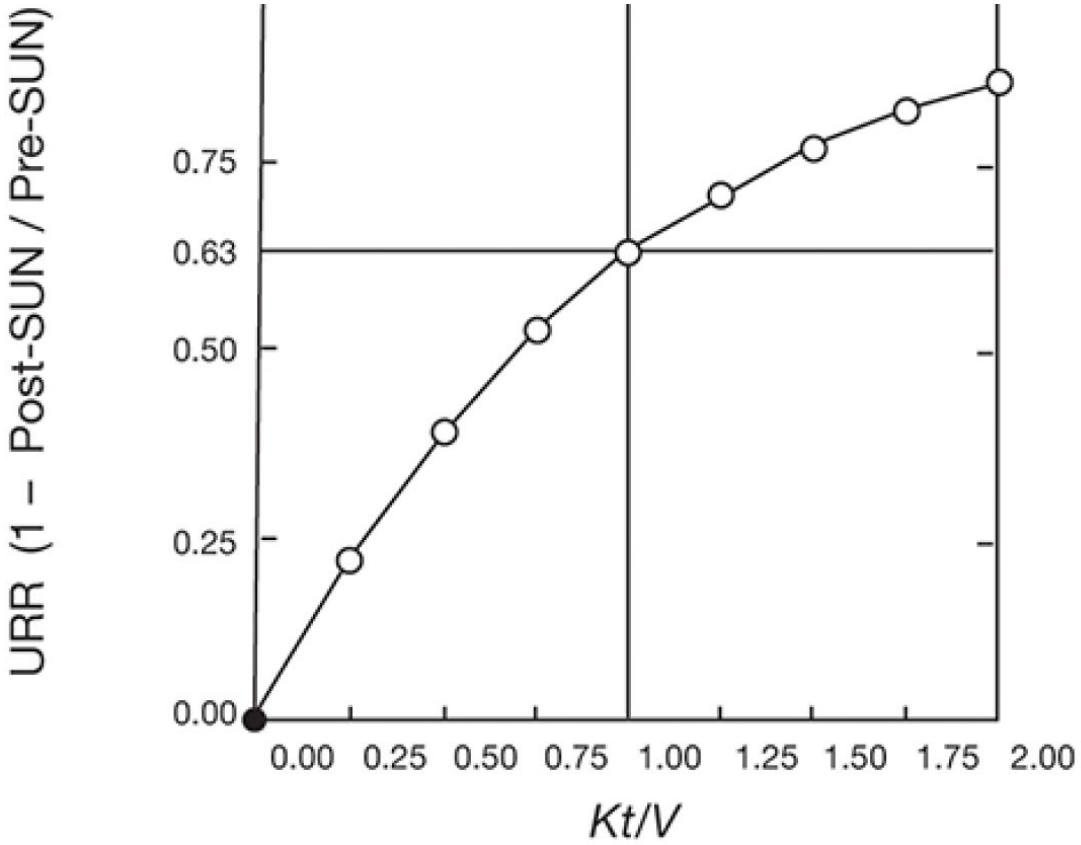
Unfortunately, each time drain tank (1L) return to tank A, C_0 each time is ***decreased (diluted)***

$$URR\% = \frac{C_0 - C}{C_0} \times 100 = \left(1 - \frac{C}{C_0}\right) \times 100$$

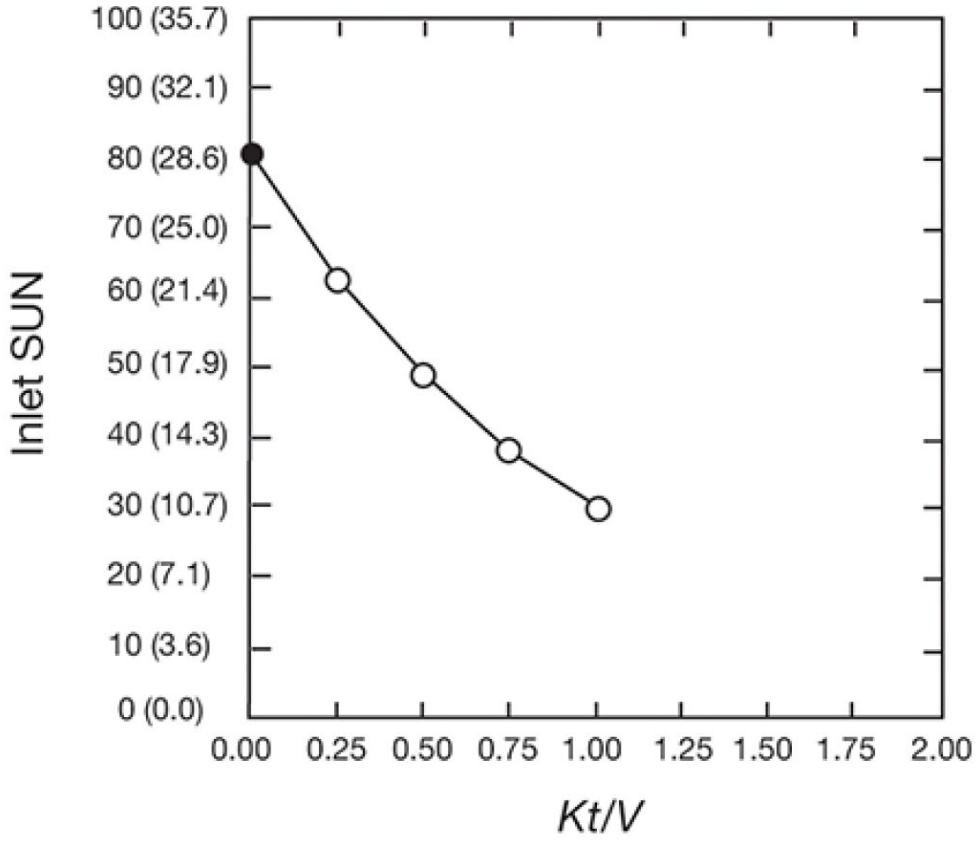
URR ≠ 1 and decreasing ***non-linearly*** *approaching 0 if long interval (i.e., CRRT)*

*URR also does not account for volume changes and urea generation

Kt/V and URR association



URR is associated with Kt/V *non-linearly*

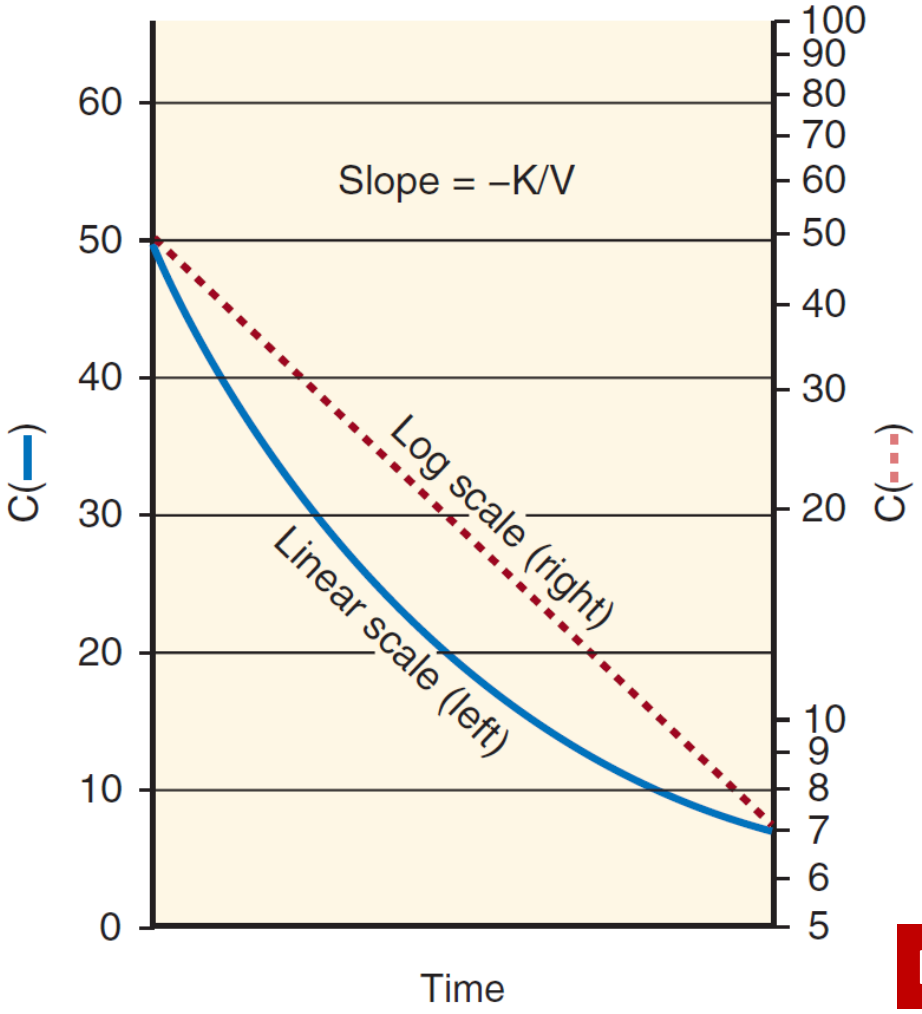


Urea fall *exponentially* with ongoing dialysis

Handbook of dialysis, 6th edition.

Kt/V and Urea concentration

1st order kinetics



k = K/V
k = *rate* constant (fractional removal)
K = clearance, V = Urea volume distribution

Assuming V is *constant* : ΔV = 0 (no urea clearance from convection)*
no urea generation during dialysis : G = 0**

$$C = C_0 e^{-kt}$$
$$C = C_0 e^{-Kt/V}$$
$$Kt/V = \ln(C_0/C)$$

We can determine *fractional clearance* if we know the *concentrations* (start and end of session)

However, if G ≠ 0, ΔV ≠ 0, $\ln(C_0/C)$ overestimate true Kt/V by ≈ 18%

Depner TA. Hemodial Int. 2005 Jul;9(3):241-54.
Brenner and Rector's the Kidney, 11th edition.
Daugirdas JT. J Am Soc Nephrol. 1993 Nov;4(5):1205-13.

Why Kt/V_{urea}

Dialysis *c*learance
Dialyzer efficiency (K_oA)
BFR
DFR

$$\frac{Kt}{V}$$

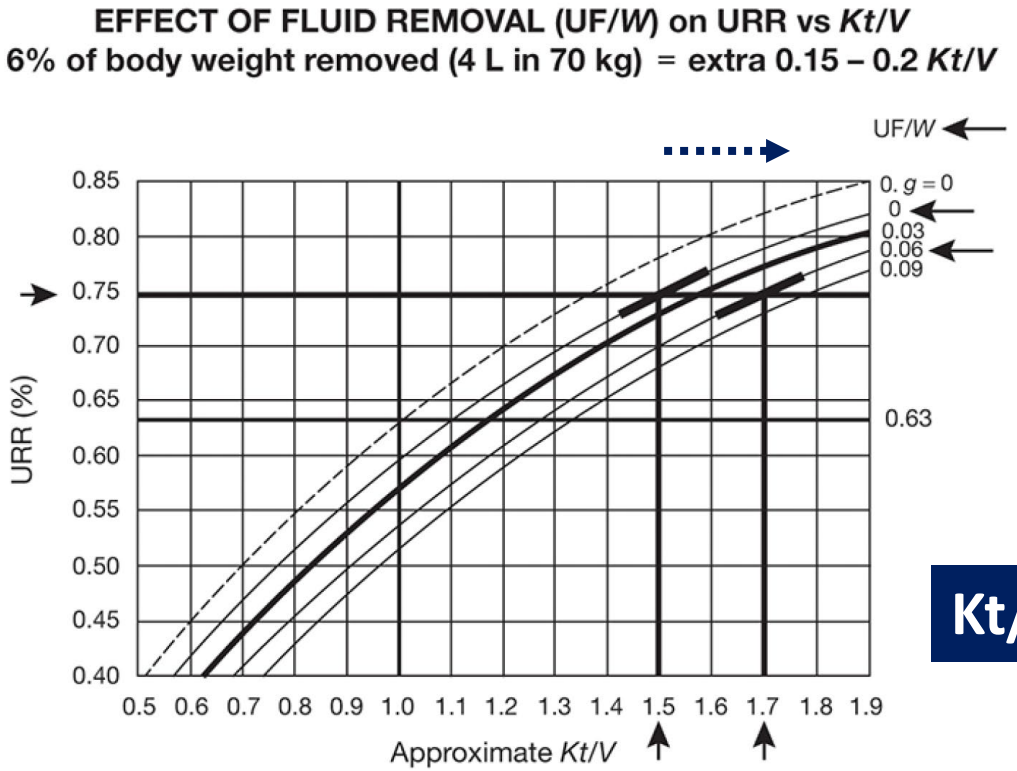
Dialysis *t*ime

***V*olume distribution of urea**
(TBW or ≈ body-size)
Age, Weight, Height, Sex

Kt/V is dimensionless & unitless
All around aspect of factors determining urea removal

Urea kinetic model: *V*olume removed

- During hemodialysis, urea removal is mediated by diffusion & ***convection*** (no changes of concentration)
- Kt/V (measure of clearance) should be accounted for convection therapy too (not only by diffusion, i.e. C_0/C or URR)



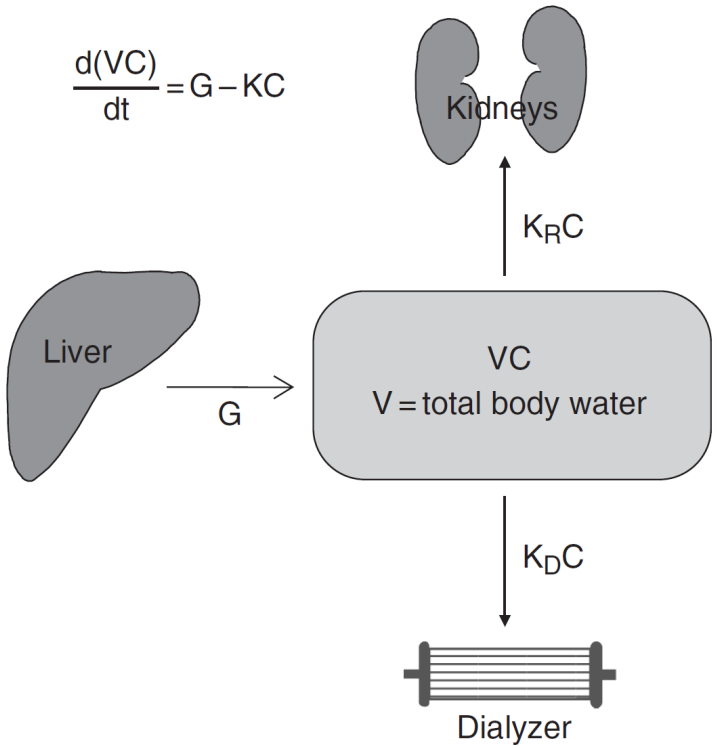
In the same URR (0.75), Kt/V increases from 1.5 to 1.7 if 6% of BW (V) is removed

Kt/V should be calculated for changes of V (UF)

Handbook of dialysis, 6th edition.

Urea kinetic model: urea *G*eneration

- During hemodialysis, urea is continuously generating from liver
- Urea concentration is not only determined by its clearance alone. Thereby, urea generation should be accounted as well esp. in *long session length*



VC = amount of urea in body (volume x concentration)
G = Urea generation from liver
KC = amount of urea clearance ($K_RC + K_DC$)

Then: $\frac{d(VC)}{dt}$ = G-KC

$$C = C_0 e^{-Kt/V}$$

$$C = C_0 \left[\frac{V_{urea} - B \cdot t}{V_{urea}}\right]^{\left(\frac{K+B}{B}\right)} + \frac{G}{K+B}\left[1 - \left[\frac{V_{urea} - B \cdot t}{V_{urea}}\right]^{\left(\frac{K+B}{B}\right)}\right]$$

B is the rate of change in Vurea (mL/min)

Depner TA. Hemodial Int. 2005 Jul;9(3):241-54.

Formal Urea kinetic model

UREAKINETICS.ORG

DIALYSIS ADEQUACY TOOLS AND CALCULATORS

Home FAQ Info

SOLUTE-SOLVER® 2-pool Kinetic Modeling Program

PATIENT DATA (*Version 2.15, June 29, 2024. Latest version at www.ureakinetics.org. Usage info at bottom of page. Browsers of choice are Chrome and Firefox.

35 inputs !!!
But can calculate: spKt/V, eKt/V, stdKt/V, G, V, nPCR, KRU, etc…

OR

SOLUTE-SOLVER® LITE

☐ Dialysis days (2-7)/wk and BUN lab day ◉

☑ Mon ○ ☐ Tue ○ ☑ Wed ◉
☐ Thu ○ ☑ Fri ○ ☐ Sat ○ ☐ Sun ○

Name:	Jiranat Sriswasdi
KRU (mL/min):	2
PREBUN(mg/dL):	80
POSTBUN(mg/dL):	30
QB (mL/min):	300
QD (mL/min):	500
TD (min):	240
PREWEIGHT(kg):	68
POSTWEIGHT(kg):	66
K_0A (mL/min):	1200

Calculate Reset

These are your results

Urea reduction ratio (%) = **62.5**
Single-pool Kt/V = **1.14**
Equilibrated Kt/V = **1.01**
DstdKt/V from dialysis only = **2.03**
stdKt/V (with 100% Kru) = **2.46**
Kru as entered (mL/min) = **2.0**

Dialyzer clearance (mL/min) = **220**
PCRn 2-pool (g/kg/day) = **1.28**
Modeled volume 2-pool (liters) = **47.1**

Lite version

www.ureakinetics.org

Daugirdas JT. Semin Dial. 2025 May-Jun;38(3):161-165.

Estimated spKt/V: Daugirdas II

The 2nd generation* logarithm *estimation* of *single* pool *variable* volume Kt/V

- *Thrice weekly* dialysis

$$\text{spKt/V} = -\ln(R - \mathbf{0.008} \times t) + (4 - 3.5 \times R) \times \frac{UF}{W}$$

R = $\frac{Post\ dialysis\ BUN}{Pre\ dialysis\ BUN}$, t = Session length (h), UF (L), W = *Post* dialysis weight (kg)

- *Non-thrice* weekly dialysis

$$\text{spKt/V} = -\ln(R - \boldsymbol{GFAC} \times t) + (4 - 3.5 \times R) \times \frac{UF}{W}$$

$$\text{GFAC (generation factor)} \approx \frac{0.0175}{Preceding\ interdialysis\ interval\ (PIDI)\ in\ days}$$

We can calculate spKt/V without the need to collect "dialyzer urea clearance" from dialysate (which is cumbersome)

*1st generation is only accurate in Kt/V < 1.3; the 2nd gen is accurate from spKt/V of 0.7-2.1

Daugirdas JT. J Am Soc Nephrol. 1993 Nov;4(5):1205-13.
Daugirdas JT, et al. Nephrol Dial Transplant. 2013 Aug;28(8):2156-60.

Urea kinetic model: calculated V_{urea}

- We (computer) can *calculate* Kt (volume of fluid cleared of urea: from K_oA, BFR, DFR, session length) which computer *assumed* to be true/fixed
- From UKM spKt/V, we can derive "urea concentration *curve*" which we then compute "**average urea concentration** during dialysis"
- So "Urea removed" = Cleared volume (Kt) x Average urea concentration
- We *directly* measure changes of Urea concentration (pre & post dialysis BUN)

$$\text{Calculated (modeled) } V_{urea} = \frac{\boldsymbol{Urea\ removed}\ (Kt \times Average\ urea\ concentration)}{\boldsymbol{\Delta BUN}\ (Pre\ dialysis\ BUN - Post\ dialysis\ BUN)}$$

Numerator: assumed data, Denominator: measured (real) data

If modeled V_{urea} ↑ (> real V) = ↓ΔBUN = false high Kt (disrupted session, recirculation, poor dialyzer)
If modeled V_{urea} ↓ (< real V) = ↑ΔBUN = false low post-dialysis BUN (early sampling)

Modeled V_{urea} should be within 90% TBW or 60-120% compared to Watson/Hume-Weyers

Handbook of dialysis, 6th edition.

Estimated spKt/V from conductivity

- **Pulse increasing of dialysate sodium** with measurement of **inlet** and **outlet** dialysate **conductivity**, one can calculate "dialysate conductive clearance" (K_{ecn}) which is similar to urea clearance

$$D = [Qd + Qf][1 - (Co_1 - Co_2)/(Ci_1 - Ci_2)]^{157}$$

Co and Ci are dialysate outlet and inlet conductivities (mS/cm); D is dialysance (mL/min); Qd is dialysate flow; and Qf is ultrafiltration flow.

- So, we now can measure K in real time (online) instead of using KoA, BFR, DFR from previous UKM
- Calibrated V_{urea} is calculated from

$$\text{Calibrated } V_{urea} = \frac{\boldsymbol{Urea\ removed}\ (\boldsymbol{K}t \times Average\ urea\ concentration)}{\boldsymbol{\Delta BUN}\ (Pre\ dialysis\ BUN - Post\ dialysis\ BUN)}$$

K_{ecn} is now from "conductivity clearance" *not* from "KoA, BFR, DFR"

Average of calibrated Vurea for a period of 6-8 months using K_{ecn} and URR*

*Post & Pre-dialysis urea is still needed to be measured in this period

KDOQI Hemodialysis Adequacy 2006.
Daugirdas JT. Semin Dial. 2018 Nov;31(6):633-636.
Raimann JG, et al. Am J Kidney Dis. 2020 Jul;76(1):22-31.
Handbook of dialysis, 6th edition.

Estimated spKt/V from conductivity

- Now we derived calibrated V_{urea} from "calibrated phase ≈ 6 months"
- In the following months (assumed **no changes of dry weight**), we now can calculate spKt/V_{cal} **without needs for "post-dialysis BUN"** measurement which is prone to error
- Pre-dialysis BUN is measured because the need to calculated nPCR
- Recalibrated (3-months) is suggested for **every 12 months** or when **dry weight is changed**

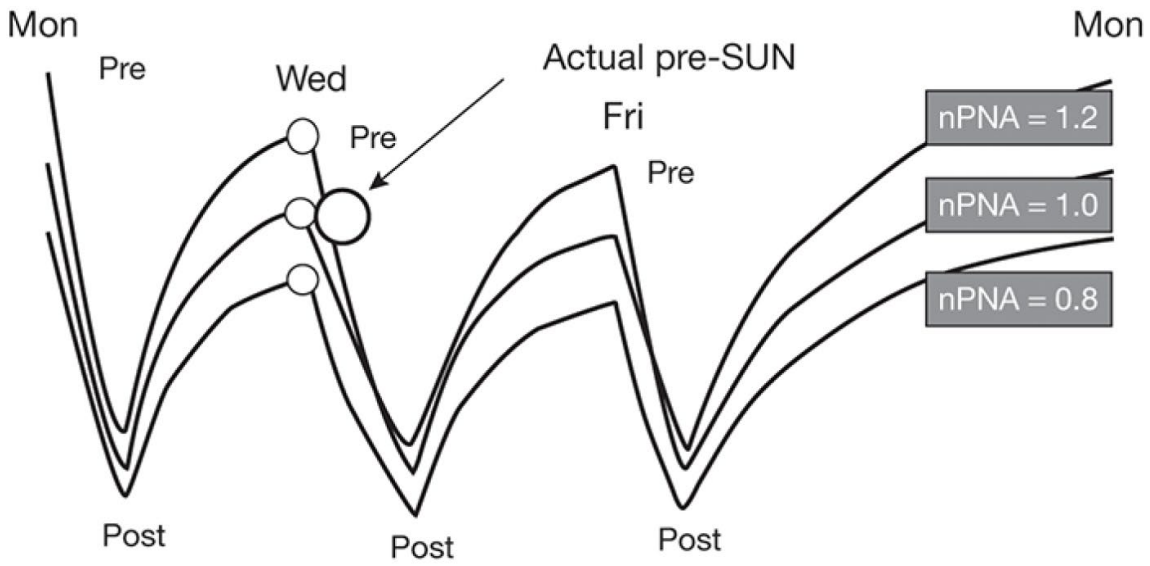
	Baseline Interval	Period 1		Period 2	
	Kt/V by Kecn_URR	Kt/V by Kecn_Vcal	Kt/V by Kecn_Vant	Kt/V by Kecn_Vcal	Kt/V by Kecn_Vant
Percent Error vs Kt/V by KdK_0A_URR[a]					
Mean ± SD	1.00 ± 0.69%	−0.63% ± 7.74%	−10.2% ± 9.78%	−0.75% ± 8.38%	−10.4% ± 9.69%
Median	0.37%	−0.55%	−10.9%	−1.02%	−11.1%
Absolute Value Percent Error vs Kt/V by KdK_0A_URR[a]					
Mean ± SD	0.59 ± 0.63	5.82 ± 5.13	12.0 ± 7.47	6.60 ± 5.22	12.1 ± 7.46
Median	0.40	4.61	11.20	5.44	11.60

Kt/V by Vcal is much more accurate than Kt/V by V using Watson model and very closed to formal UKM

Daugirdas JT. Semin Dial. 2018 Nov;31(6):633-636.
Raimann JG, et al. Am J Kidney Dis. 2020 Jul;76(1):22-31.

Urea kinetic model: nPCR

From UKM, we can utilize calculated V_{urea} and Pre-dialysis Urea plotting graph for which nPCR best suited for “measured” pre-dialysis urea



In this example, nPNA 1.2 is selected due to best matched for actual pre-SUN

However, multiple formulas for nPCR exist…

midweek PNA (PCR, g/day) = pre-dialysis BUN/ [25.8+ ((1.15)/(spKt/v)] + 56.4/(spKt/v)] +0.168 สำหรับผู้ป่วยฟอกเลือด 3 ครั้ง/สัปดาห์ที่ไม่มีปัสสาวะหลงเหลืออยู่ และ normalized PNA (nPCR), g/kg/day = (PNA)/(V/0.58)

nPCR = 0.22 + $\left(\frac{0.36\times(predialysis\ BUN - PostdialysisBUN)\times 24}{Interdialytic\ interval\ (h)}\right)$

OR

nPCR = (0.0136 x F) + 0.251

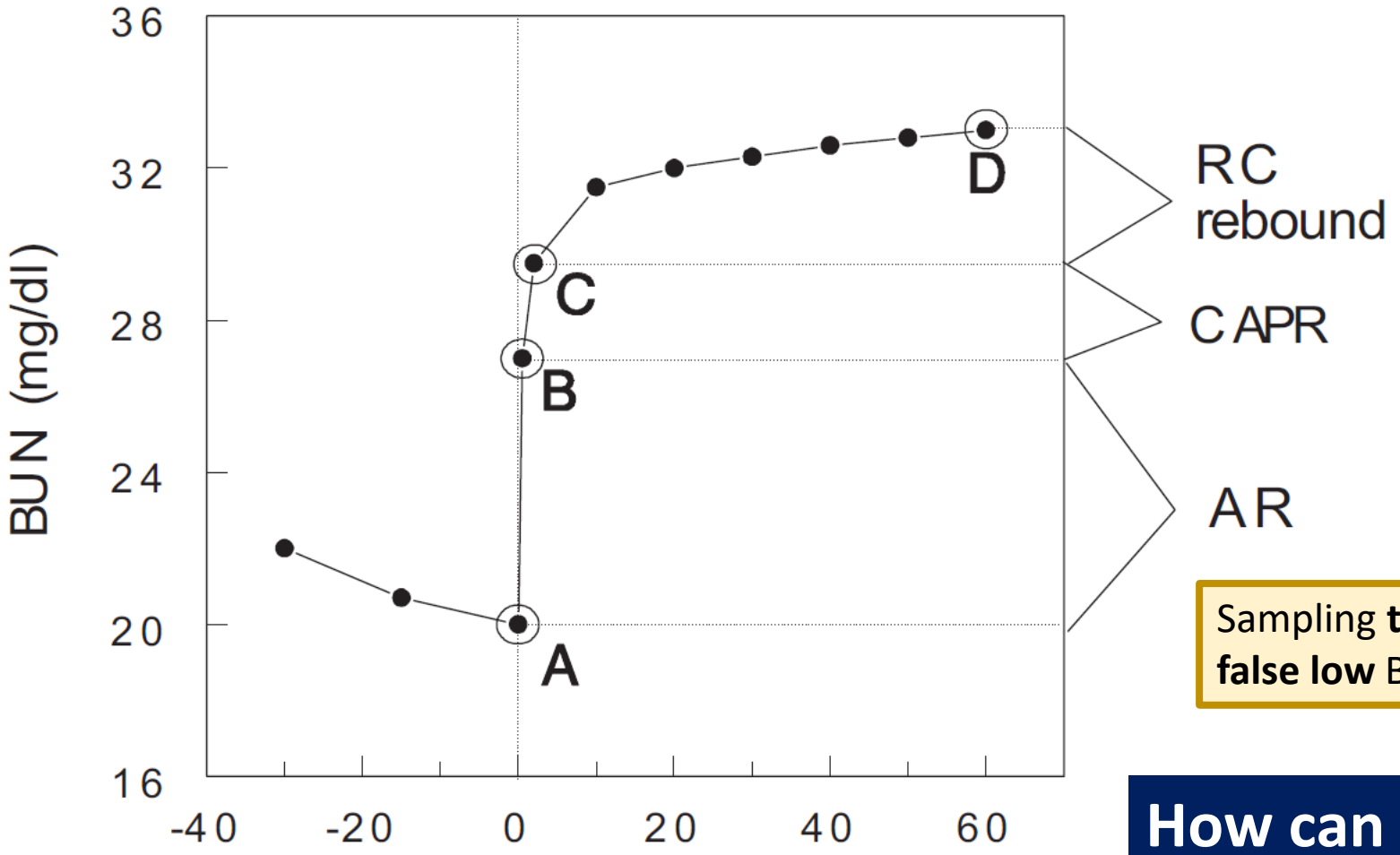
F = Kt/V $\left(\frac{Predialysis\ BUN + Postdialysis\ BUN}{2}\right)$

+ urine nPCR = $\frac{UUN(g)\ x\ 150}{Interdialytic\ interval\ (h) x\ weight\ (kg)}$

However, PCR overestimated if protein intake < 1 g/kg/d
And underestimated if protein intake > 1 g/kg/d
High if hypercatabolic or low if anabolic state (recover phase)

Thai SPENT 2020
NST 2022
KDOQI guideline 2020
Handbook of dialysis, 6th edition.

Urea rebound: post-dialysis BUN



3 types of Post-dialysis urea rebound

1.Access recirculation
A→B: **first 20 seconds**
2.Cardiopulmonary recirculation
B→C: 20s to **3 minutes**
3.Remote compartment rebound
C→D: 3 minutes to **30-60 minutes**

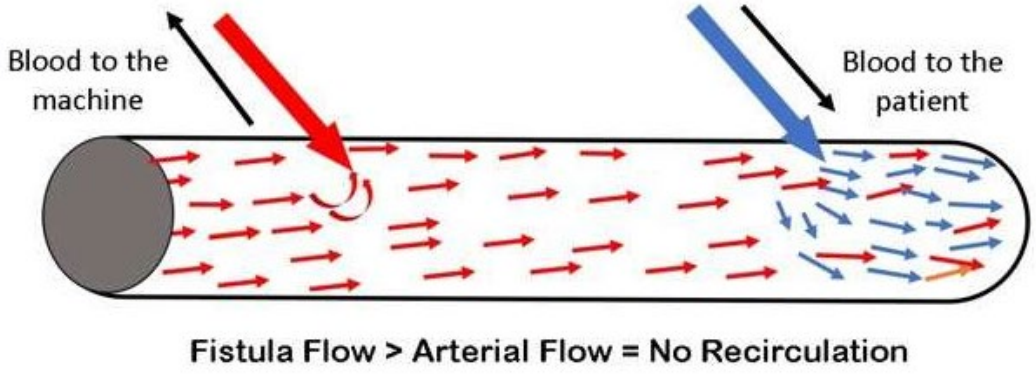
Sampling **too early** (right away after dialysis) results in **false low** BUN = **false high** URR or spKt/V

How can we eliminate these effects?

KDOQI Hemodialysis Adequacy 2006.

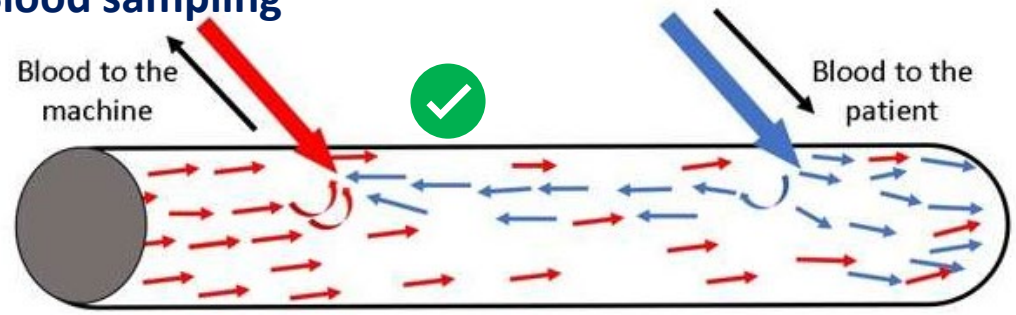
Access recirculation (AR)

Blood sampling



Fistula Flow > Arterial Flow = No Recirculation

Blood sampling



Fistula flow < arterial flow = Recirculation

Non-dialyzed blood Dialyzed blood

Can occur in ***CVC*** as well

To eliminate the effect of access recirculation

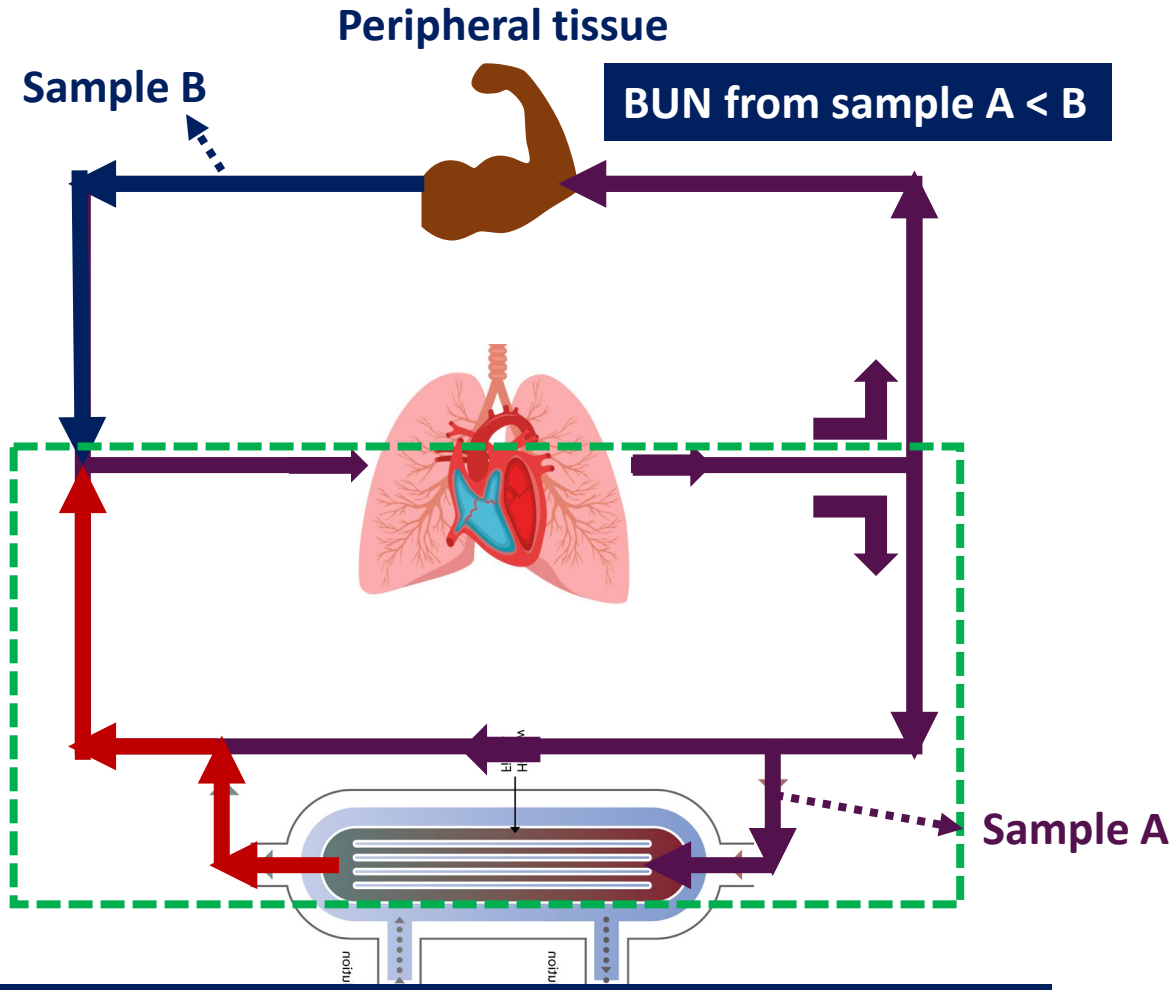
Method 1: **Slow BFR** to 100 mL/min for 15 sec (25 mL) to
1) Assuredly ***BFR is lower*** than ***Access flow*** rate
2) Blood flow into the inlet is not recirculated blood
3) 25 mL is adequately more than dead space of needle tip to sampling port
Make sure UFR = < 50 mL/h, DFR = 0

Method 2: **Stop DFR** (same BFR) to for 3 minutes to
1) Assuredly **same BUN** of **dialyzed** blood and **inlet** blood
2) Trapped dialysate is needed to be quickly equilibrated with blood, so BFR should not be slow
Make sure UFR = < 50 mL/h but ***SAME BFR***

Method 2 eliminates CAPR as well and results in more post-dialysis BUN (modestly) than method 1

KDOQI Hemodialysis Adequacy 2006.

Cardiopulmonary recirculation



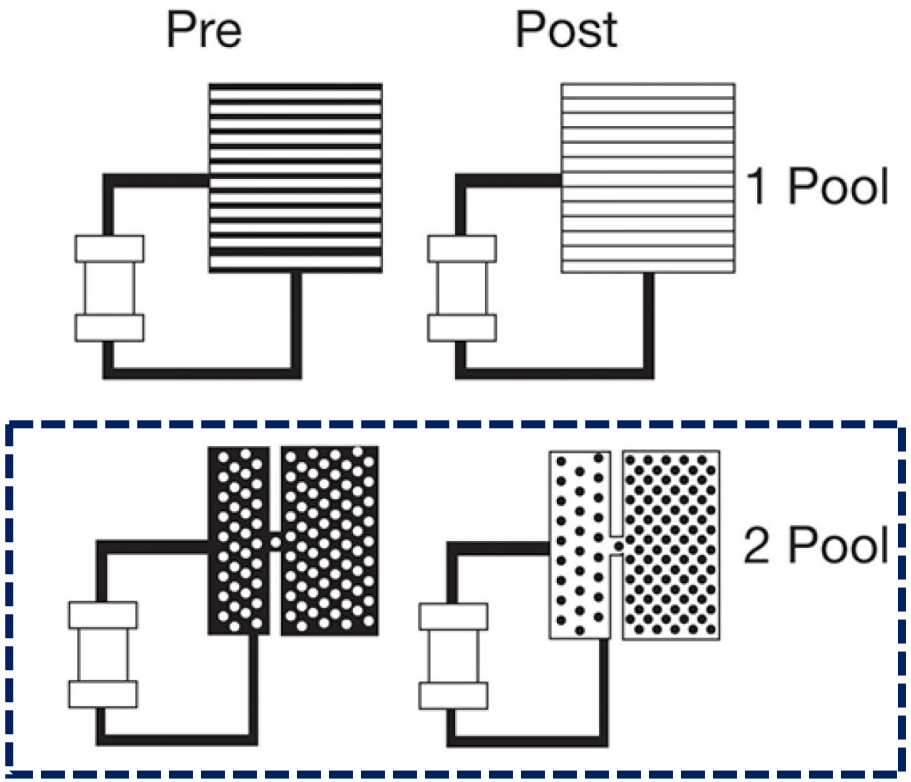
- In case of CVC, all blood going through extracorporeal circuit is from vein which must be from peripheral tissue.
- **No cardiopulmonary recirculation in CVCs.**

To eliminate cardiopulmonary recirculation, **stop DFR for 3 minutes** results in equalization of sample A and B but results in **lower spKt/V** (modestly)

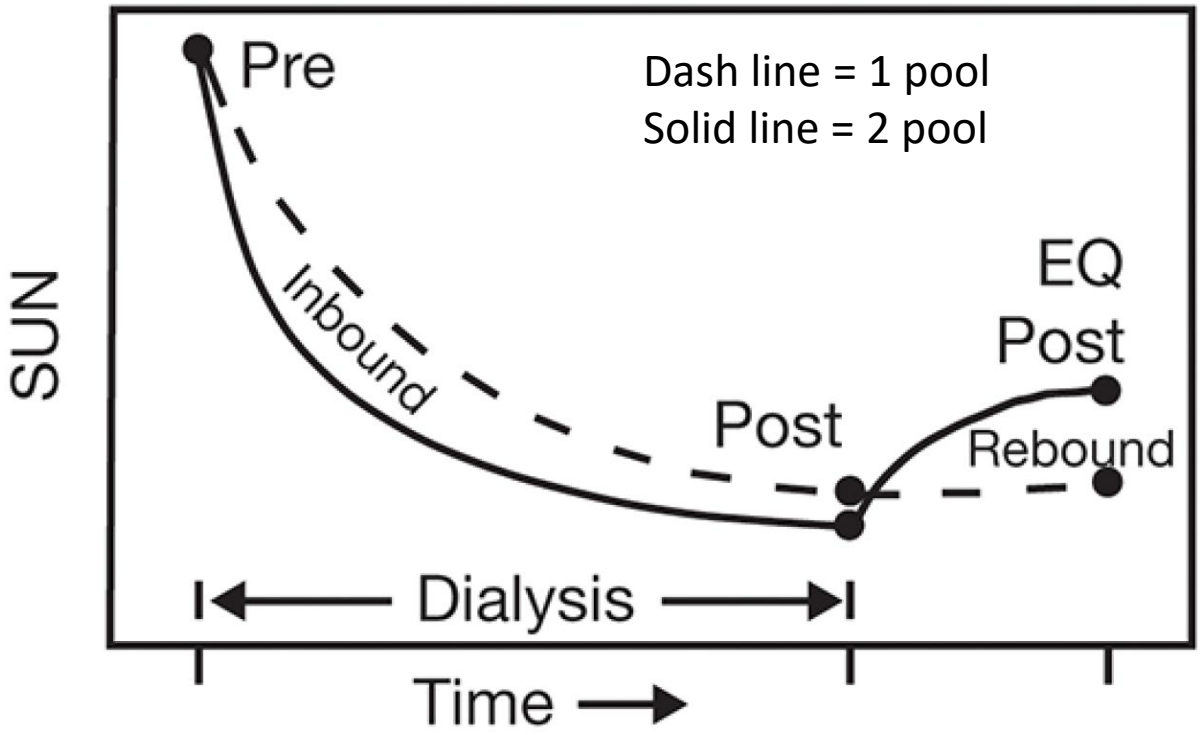
Some part of blood passing through cardiopulmonary circulation without going to peripheral tissue

KDOQI Hemodialysis Adequacy 2006.
Handbook of dialysis, 6th edition.

Double pool (compartments) model



Intracellular urea is not fast enough to move outside to vascular space (dialyzable area) and after dialysis ends it **slowly distributed intravascularly in 30-60 mins**



During dialysis BUN is ***lower*** in double pool model due to smaller compartment of urea distribution **(urea inbound)**
After dialysis BUN is ***higher*** due to urea flux outside cell/tissue **(urea rebound),** these 2 effects **cancel each other** making modeled V_{urea} still correct

Handbook of dialysis, 6th edition.

Equilibrated Kt/V (eKt/V)

- Equilibrated Kt/V referred to Kt/V_{urea} using urea that is **equilibrated for double pool** model (≈ 30 mins blood sampling with slow BFR 15s)
- Generally, **eKt/V** is ***lower*** than **spKt/V** (because post-dialysis in eKt/V is higher) but degree of difference depends on ***session length*** and ***intensity*** (relative to body size)

sp*Kt/V*	*t*(h)	sp*Kt/V* per h	Rebound	e*Kt/V*
1.2	6	0.2	0.09	1.11
1.2	3	0.4	0.17	1.03
1.2	2	0.6	0.24	0.96

Shorter time or high spKt/V per h (intensity) results in higher rebound and lower eKt/V

Handbook of dialysis, 6th edition.

Equilibrated Kt/V (eKt/V)

- Estimating equilibrated Kt/V from spKt/V
- Tattersall formula
  - **eKt/V = spKt/V x ($\frac{Td}{Td+35}$), Td = session length (minutes) if AVF**
  - eKt/V = spKt/V x ($\frac{Td}{Td+22}$) if **CVC**
  - Some suggest Td+30.7 (according to HEMO study)
- But generally, **eKt/V is lower than spKt/V ≈ 0.2**
- ***No study*** existed, whether eKt/V is better than spKt/V
- eKt/V maybe preferred in those with **short dialysis,** those with **slow urea distribution** (low cardiac output), or high intensity relative to V

Handbook of dialysis, 6th edition.
KDOQI Hemodialysis Adequacy 2006.
Depner TA. Hemodial Int. 2005 Jul;9(3):241-54.

HEMO trial: is dose matter?

1,846 HD adults, mean dialysis vintage 3.7 years, mean nPCR 1.0 g/kg/d, albumin 3.6 g/dL, **KRU < 1.5 mL/min**
HD 3 sessions/week at least 2.5 h/session

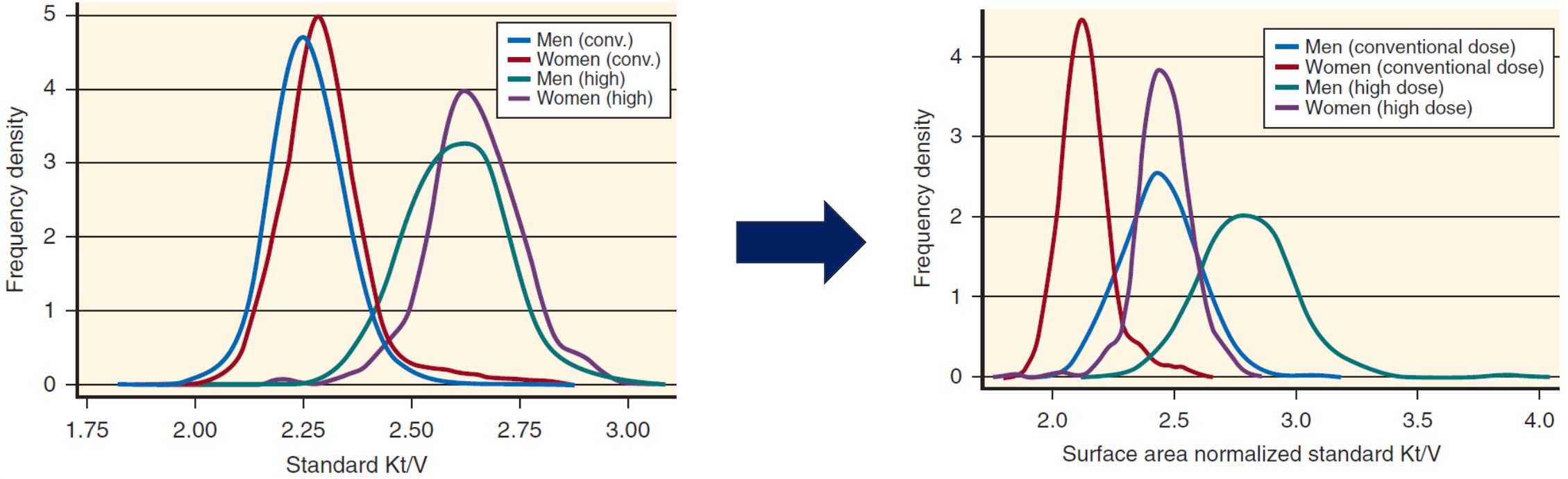
2x2 tables	**Standard dose** eKt/V 1.05 (spKt/V 1.25) URR 65%	**High dose** eKt/V 1.45 (spKt/V 1.65) URR 75%
Low flux β2-microlobulin clearance < 10 mL/min	**Group A**	**Group B**
High flux β2-microlobulin clearance > 20 mL/min & K_{UF} > 14 ml/h/mmHg	**Group C**	**Group D**

1˚ outcome = death from any cause

Overall; ***no significant difference*** **between standard vs high dose and high vs low flux**
However, in **high vs low flux**; those with **vintage > 3.7 y** benefit from high flux
In **high vs standard dose**; **female** with high dose has lower mortality than those with low dose

Eknoyan G, et al. N Engl J Med. 2002 Dec 19;347(25):2010-9.

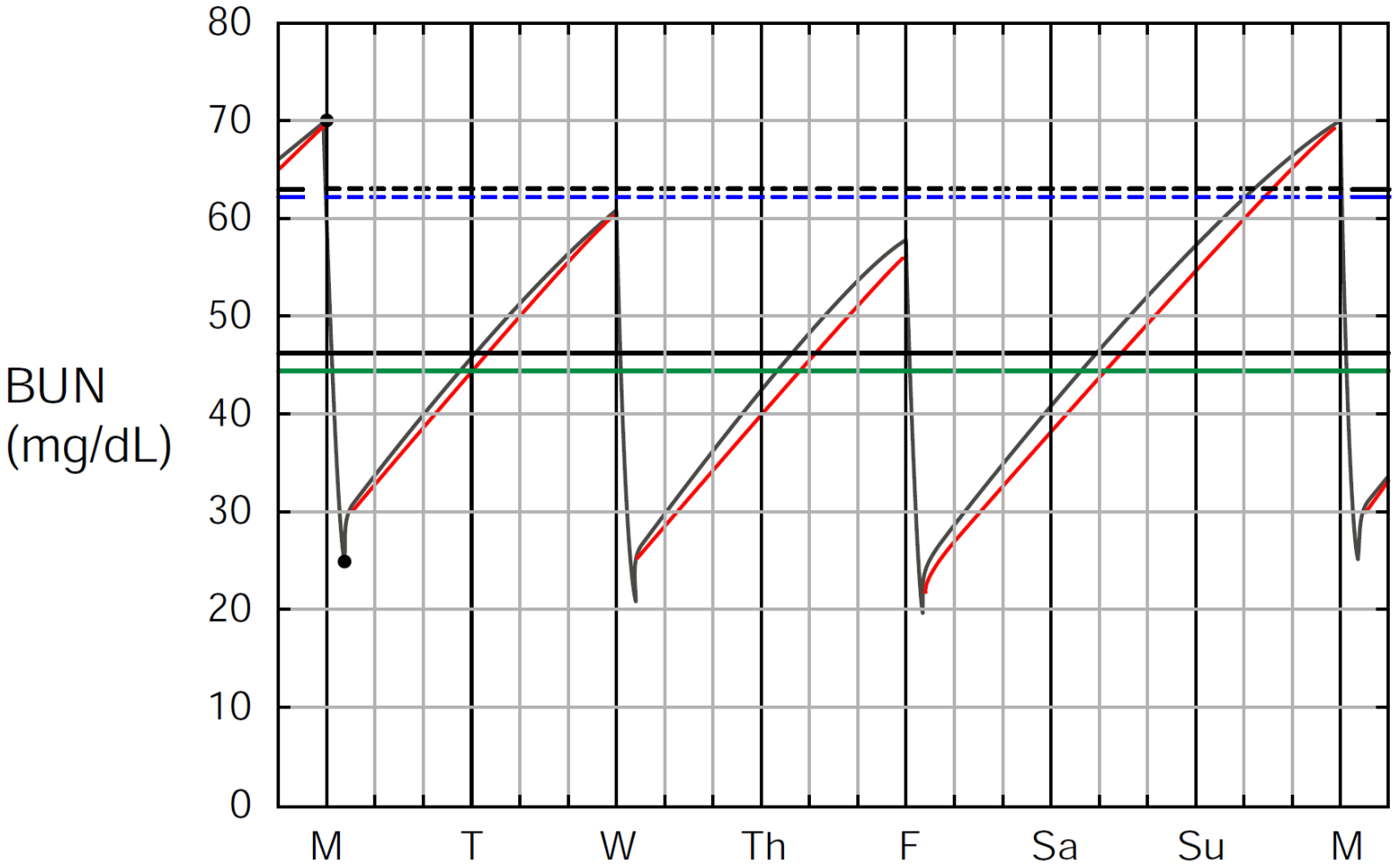
V or BSA for standardization



- Woman comparing to man, has **lower V/surface area ratio** (lower muscle mass)
- If normalized for surface area, **Kt/V of woman in HEMO study** (conventional dose) is significantly **low**
- However, surface area normalizing is not routinely practice due to highly varied height & weight.

Eknoyan G, et al. N Engl J Med. 2002 Dec 19;347(25):2010-9.
Daugirdas JT, et al. Clin J Am Soc Nephrol. 2010 Sep;5(9):1628-36.

Residual kidney function on UKM



UKM from **HD 3/week** with or without KRU
With KRU: black saw-tooth BUN, green TAC and blue dash line pre-dialysis BUN
Without KRU: red saw-tooth BUN, grey TAC and black dash line pre-dialysis

Modeled G and modeled nPCR are ↓ if not accounted *KRU*

Handbook of dialysis therapy, 6th edition.

Renal + dialysis clearance?

- 2 methods (Renal clearance is *continuous* and dialysis is *intermittent*)
  - 1) Make Renal clearance into intermittent form then adding to dialysis clearance (possible ***but cumbersome***)
  - 2) Make **Intermittent dialysis clearance into continuous** data then combined with renal clearance (easier and can be compared with peritoneal dialysis which is continuous)

Handbook of dialysis, 6th edition.
KDOQI Hemodialysis Adequacy 2006.

Calculating KRU

- Renal urea clearance is determined from
  - KRU (mL/min) = $\frac{Urine\ urea\ nitrogen\ (UUN)\ mg/dL}{\boldsymbol{Average\ SUN\ during\ collection\ (TAC)\ mg/dL}}$ x Urine flow (mL/min)

Determining TAC

(plasma water concentration)

1) **Formal UKM (ureakinetic.org)**
2) Average of Post-dialysis SUN and Predialysis SUN
3) 0.25 U1 + 0.75 U2…if 3/week, 0.16 U1 + 0.84 U2…if 2/week
(U1 = Post 1st dialysis SUN, U2 = Post 2nd dialysis SUN)
4) R = 1.075 - (0.0038 x URR + 0.059) x UDUR (min)/IDI (min)
then R x Predialysis SUN = TAC
UDUR = duration of urine collection, IDI = Interdialytic interval
5) **Daugirdas method: 0.9 x Predialysis SUN** (0.85 for plasma UN**, 0.9 for plasma water UN**)

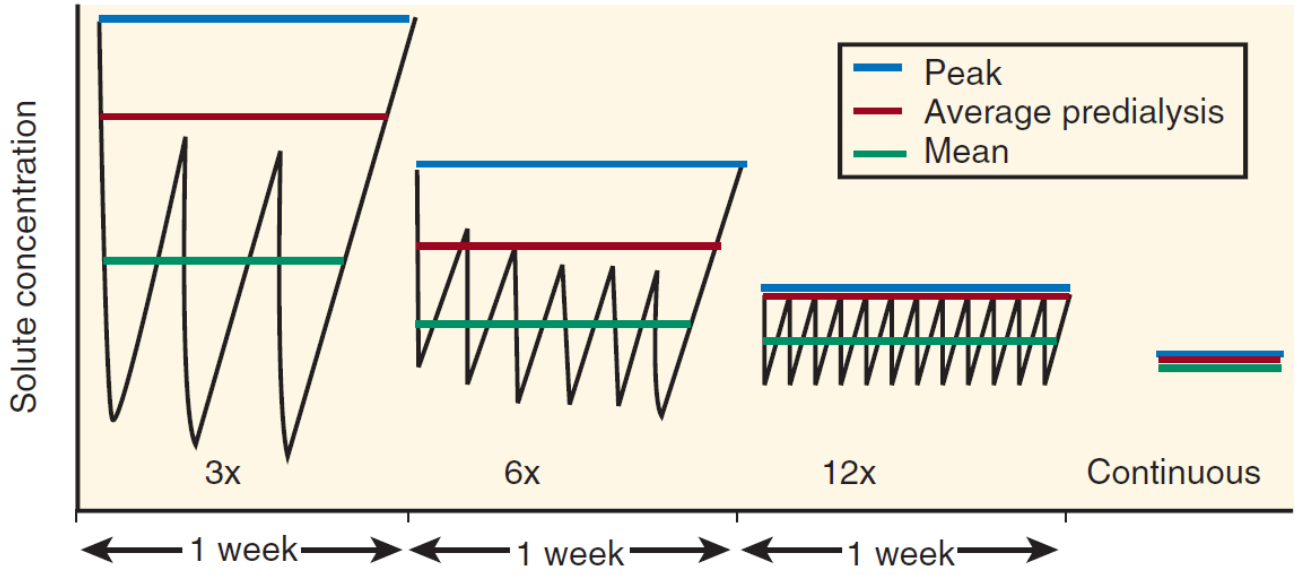
TABLE 1. Ratio of TAC to predialysis BUN for a conventional 3/week or a 2/week schedule and various collection periods

Duration of urine collection	URR (%)	Interdialytic interval	
		2 days	3 days
~24 hours	63	0.92	0.98
	75	0.89	0.96
~44 hours	63	0.78	0.87
	75	0.72	0.83
~68 hours	63	NA	0.78
	75	NA	0.72

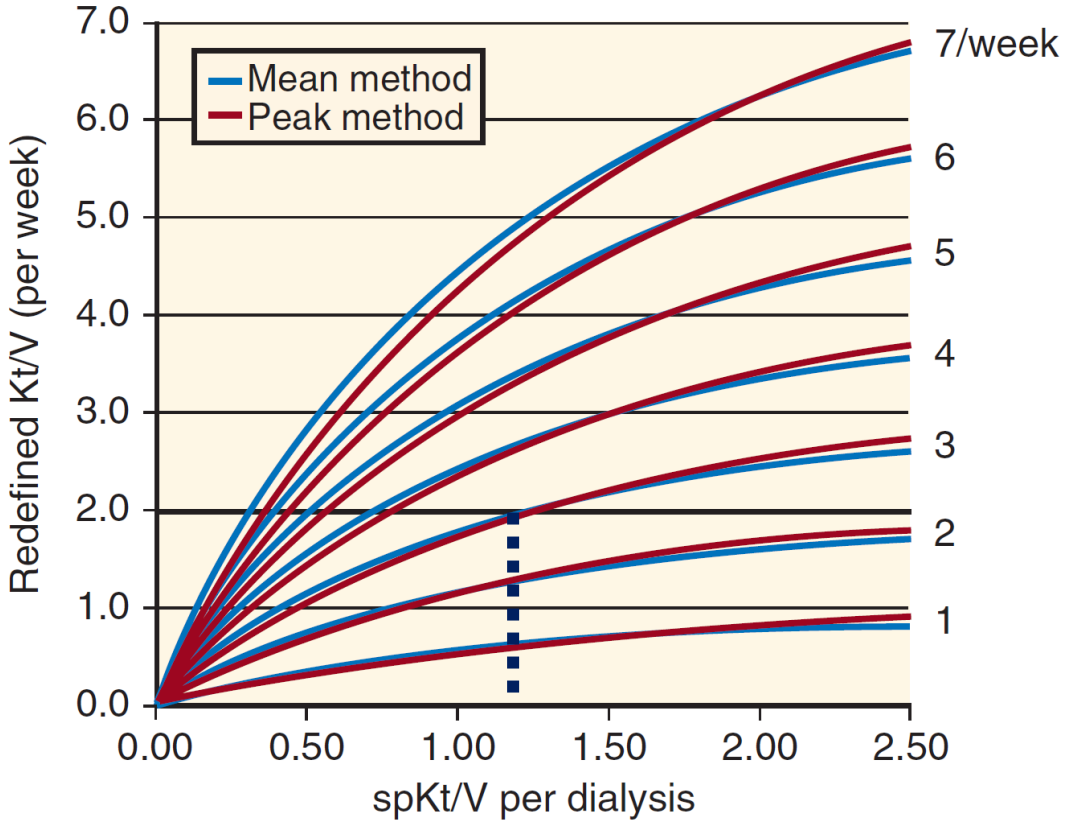
Ratio to convert Predialysis BUN to TAC

Chin AI, et al. Semin Dial. 2017 May;30(3):235-240.
NST 2022.

Non-thrice weekly dialysis?



Despite **same Kt/V per session** and ***decreasing*** URR
Peak BUN, Average BUN, Mean BUN is lower in more frequent or continuous group



In those with spKt/V 1.2 x3/week. Weekly Kt/V = 2
Which is **impossible if frequency x2/week** (no urine)

Frequency affect solute clearance independent of intensity of dialysis per session

Brenner and Rector's the Kidney, 11th edition.

Standard Kt/V (stdKt/V)

- We need a parameter for dialysis adequacy accounted to
  - **Residual kidney function** (continuous data),
  - **Non-conventional HD** method (frequent or long session),
  - And to compared with other modalities (**Peritoneal dialysis**)

- So, Kt/V that is **continuous** and can be adding simultaneously with KRU is termed **standard Kt/V** which takes **1 week period** (contrast to previous spKt/V or eKt/V which takes **1 session**)

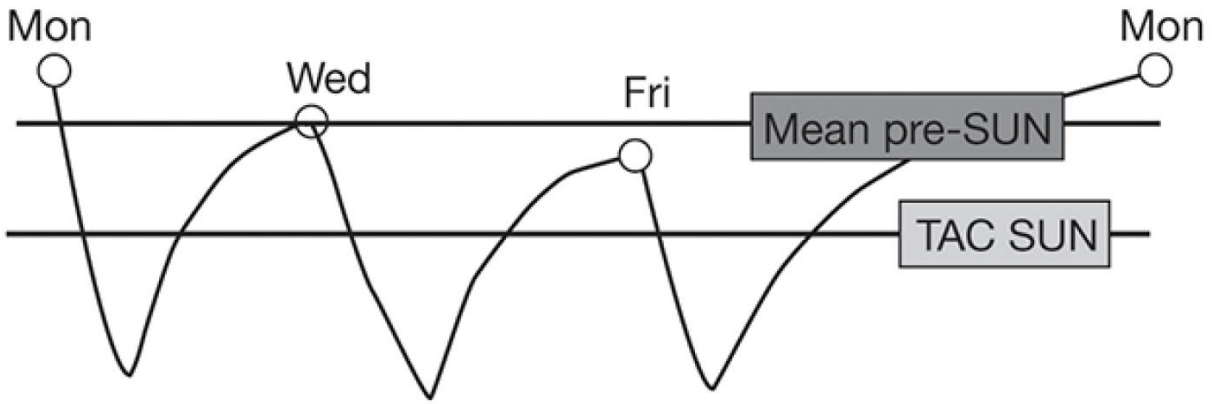
KDOQI Hemodialysis Adequacy 2006.
KDOQI Hemodialysis Adequacy 2015.
Handbook of dialysis, 6th edition.

stdKt/V & EKRU: continuous clearance

- **Equivalent renal clearance**
  - EKRC = $\frac{Urea\ removal}{\boldsymbol{TAC}}$ (in stable state urea removal = urea generation (G))

    EKRC = $\frac{G}{\boldsymbol{TAC}}$ ml/min……..We can calculate G and TAC from formal UKM

  But if spKt/V 1.2 x 3/weeks then EKRC ≈ 11 mL/min for V = 35, we will get equivalent Kt/V 3.1 which is higher than weekly Kt/V of PD (≈ 2)
- **stdKt/V**
  - High weekly Kt/V from EKRC is contributed to **TAC which is lower than mean Pre-dialysis SUN**
  - **stdKt/V** = $\frac{G}{\boldsymbol{Mean\ weekly\ predialysis\ SUN}}$; stdKt/V is closely related to PD weekly Kt/V



Mean pre-SUN **is higher** than TAC
stdKt/V ≈ 1/3 lower

Handbook of dialysis, 6th edition.

stdKt/V derivation from spKt/V

- Formula (1) $eKt/V = spKt/V \times \frac{T}{(T+30.7)}$

- Formula (2) $$stdKt/V = \frac{10{,}080\,\frac{1-e^{-eKt/V}}{t}}{\frac{1-e^{-eKt/V}}{eKt/V} + \frac{10{,}080}{Nt} - 1}$$

Fixed volume, no KRU

eKt/V is from formula (1), N or F is for number of dialysis per week, t is HD time (minute)

- Formula (3) $$stdKt/V = \frac{S}{1 - \frac{0.74}{F}\left[\frac{U_f}{V}\right]} + K_r\frac{10{,}080}{V}$$

Variable volume model with KRU

S is for stdKt/V of formula (2), U_f is volume removed/week

Final Formula

$$stdKt/V = \frac{\left(\frac{10080 \times \frac{1-e^{-eKt/V}}{t}}{\frac{1-e^{-eKt/V}}{eKt/V} + \frac{10080}{F \times t} - 1}\right)}{\left(1 - \frac{0.74}{F} \times \frac{UF_w}{V}\right)} + \left(K_R \times \frac{10080}{V}\right)$$

KRU 3 mL/min ≈ stdKt/V 1 volume/week

KDOQI Hemodialysis Adequacy 2015.
Handbook of dialysis therapy, 6th edition.

Guidelines for Kt/V

KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
National Kidney Foundation

NEPHROLOGY

- **Target spKt/V** of **1.4**[A] for ***thrice*** weekly with minimum **spKt/V 1.2** *,**
- If no spKt/V then use URR target **70%** and delivered **65%****
- If ***twice*** weekly and **no** urine, target **spKt/V 2.1** and delivered **> 1.8**** (But in ***KDOQI 2006, KRU < 3 mL/min; twice weekly should be avoid)
- In patient with significant KRU (**> 2** mL/min/1.73 m^2***), dialysis dose maybe reduced if KRU is measured periodically
- For those dialysis schedule is ***not thrice weekly***, target weekly **stdKt/V** should be **2.3** (2.4**) and minimum delivered **2.1***,** or EKRc ≥ 12 mL/min/35L**

A: Target 1.4 is to make sure that < 10% of treatment is lower than 1.2; data from HEMO study*** and targeting > 15% higher than minimum

*KDOQI Hemodialysis Adequacy 2015.
**NST 2022.
***KDOQI Hemodialysis Adequacy 2006.

Guidelines for monitoring

KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
National Kidney Foundation

NEPHROLOGY

- **Kt/V** should be assessed q 1 month*** or at least **3** months**

Type of dialysis	Frequency of KRU
Incremental dialysis	Q 3 months
2/week: adequate	Q 4-6 months
2/week: inadequate	When inadequate
3/week: adequate	No need
Urine < 100 mL/d or CrCl < 1 mL/min	No need

*KDOQI Hemodialysis Adequacy 2015.
**NST 2022.
***KDOQI Hemodialysis Adequacy 2006.

spKt/V accounting for KRU

KDOQI
KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
National Kidney Foundation

NEPHROLOGY

Minimum spKt/V[a] Values Corresponding to a stdKt/V[b] of Approximately 2.0 per Week

Schedule	K_r <2 mL/min/1.73 m²	K_r >2 mL/min/1.73 m²
2x/wk	Not recommended	2.0[c]
3x/wk	1.2	0. 9
4x/wk	0.8	0.6
6x/wk (short daily)	0.5	0.4

a. Dialyzer clearance only, expressed per dialysis

b. Calculated using a 2-compartment mathematical model. Assumptions: patient with V = 35 L (should not matter); T_d is constant; K_d varies; ultrafiltration is 7 L/wk; nPCR is 1 g/kg/d (should not matter); dialyzed compartment is 1/3 of total V; K_r(urea) is 0 or 2 mL/min; symmetric schedule. (old formula, not accounted for UF and KRU > 2)

c. Not recommended unless Kr > 3

It is important to note that the minimum values for spKt/V shown in this table do not take into account reported improvements in outcome from increasing Kt/V when dialysis frequency is increase to more than 3x/week.

If spKt/V 1.2 and HD 3/week without KRU, stdKt/V is ≈ 2 (actually, 2.1 based on newer formula)
So, **the minimum stdKt/V is 2.0 (2.1)** and ***spKt/V can be lowered*** **if** ***adequate KRU*** **&** ***adequate frequency***

KDOQI Hemodialysis Adequacy 2006.

Kt/V_{urea} limitations

- Controversy evidence of **toxicity** from urea (in vivo; human)
- Raising Kt/V **above standard dose** does not improve outcome in RCT
- Urea kinetic differs from **another uremic** toxins
- UKM does not concern benefit of **high flux** or **convection therapy**
- Kt/V_{urea} does not solely explain benefit of ***renal*** **clearance**
- Incompletely considers of longer session benefit
- Does not reflect other dialysis technique which affect on mortality **(UF rate, dialysate Na, Ca, K)**
- Index of **V is varied** and can be disturbed by abnormal body composition

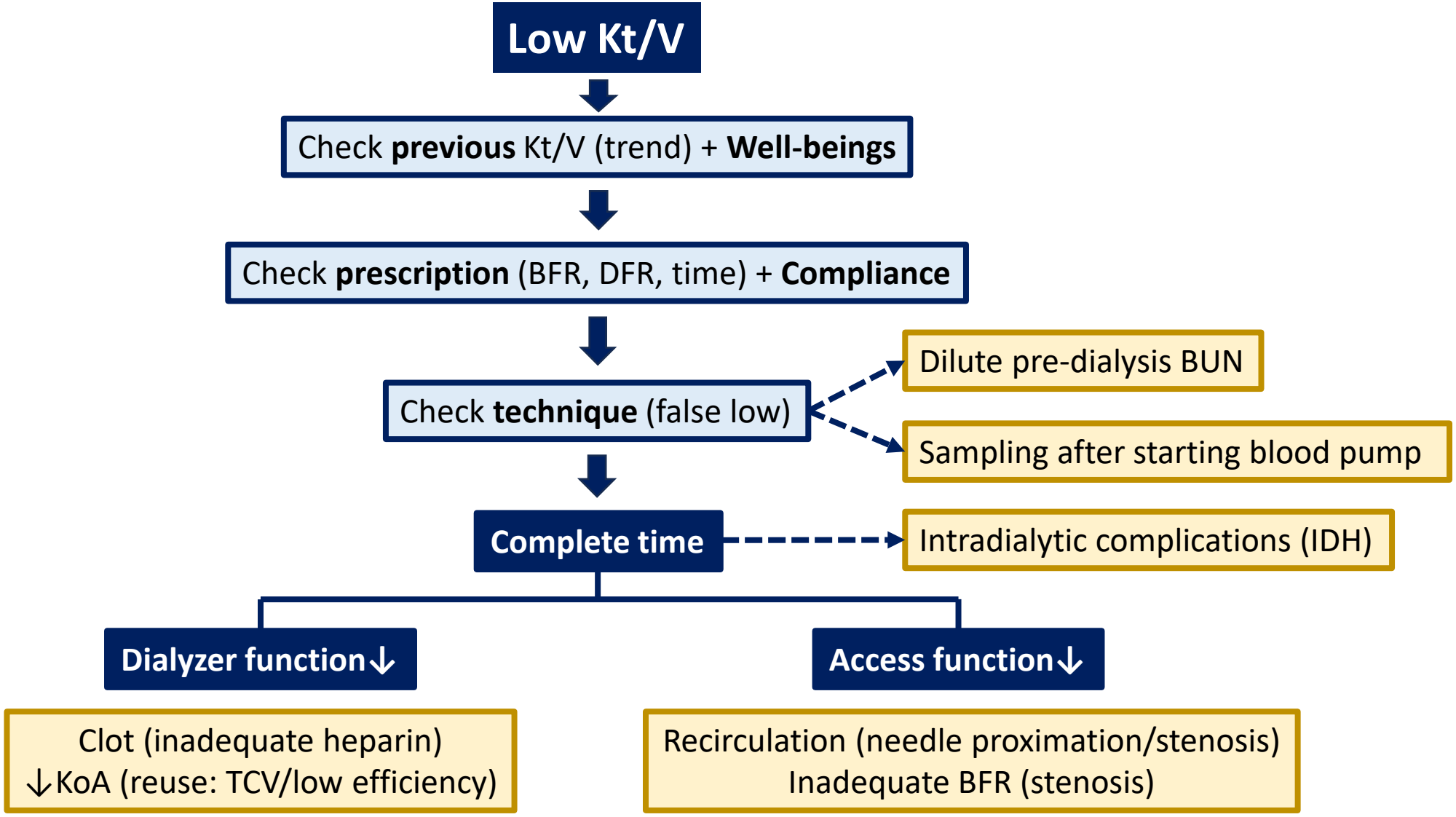
Vanholder R, et al. Kidney Int. 2015 Sep;88(3):460-5.
Vanholder R, et al. Semin Dial. 2019 Sep;32(5):424-437.

Approaching unexpecting Kt/V

Problem	Possible causes
Too high Kt/V or Modeled V < V anthropometry (Watson)	Almost always attributed to drawing the sample from the venous rather than arterial port Dilution of postdialysis blood sample with injected saline or transfused blood
No slow BFR or stop DFR prior to sampling	
False low V (malnutrition) or high intensity in small V	
Too low Kt/V or Modeled V > V anthropometry	Access recirculation Wrong dialyzer or incorrect K_0A Undetected early termination of treatment Dialyzer clotting or loss of surface from reuse Reversal of blood/dialysate flow directions Wrong or nonoccluding blood pump segment Inaccurately calibrated blood pump Drawing the predialysis sample after starting the blood pump intradialysis infusions of parenteral nutrition
Dilution of pre-dialysis BUN sampling	
PCRn lower than expected	Underestimation or nonrecognition of Kr **Or recover phase**
PCRn higher than expected	**Hypercatabolic/**Overestimation or failure to recognize loss of Kr

Depner TA. Hemodial Int. 2005 Jul;9(3):241-54.

Approaching low Kt/V

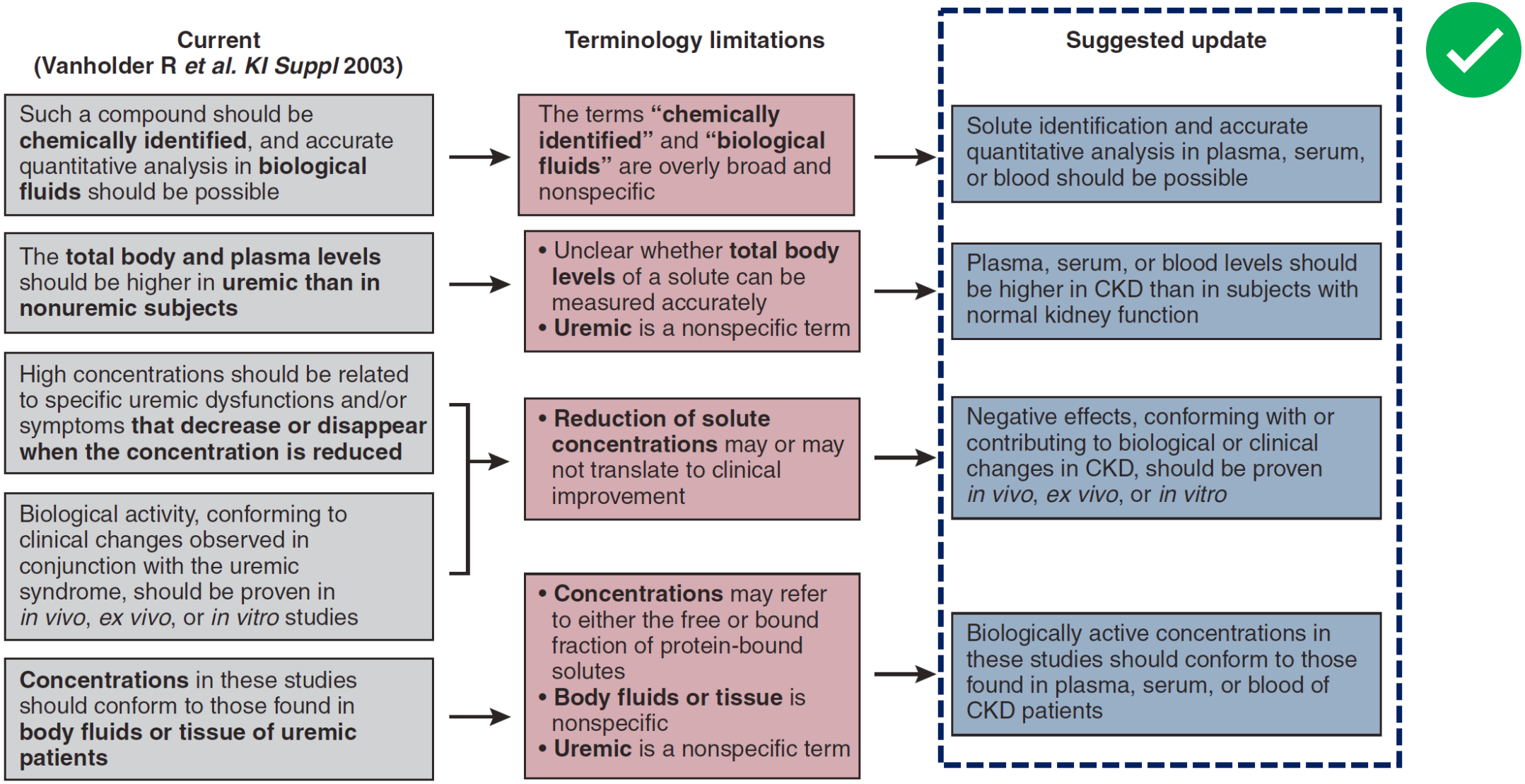


Take home message

- Improving dialysis patient outcome should be *comprehensively* done in both clinical, patient & caregiver aspects
- *Urea ≠ ideal uremic toxin* for adequacy, but no other toxins are more validated or practical
- *Kt/V* is the most practical and standard adequacy assessment with *some limitations*
- Kt/V should always be assessed concurrently with *clinical evaluation*

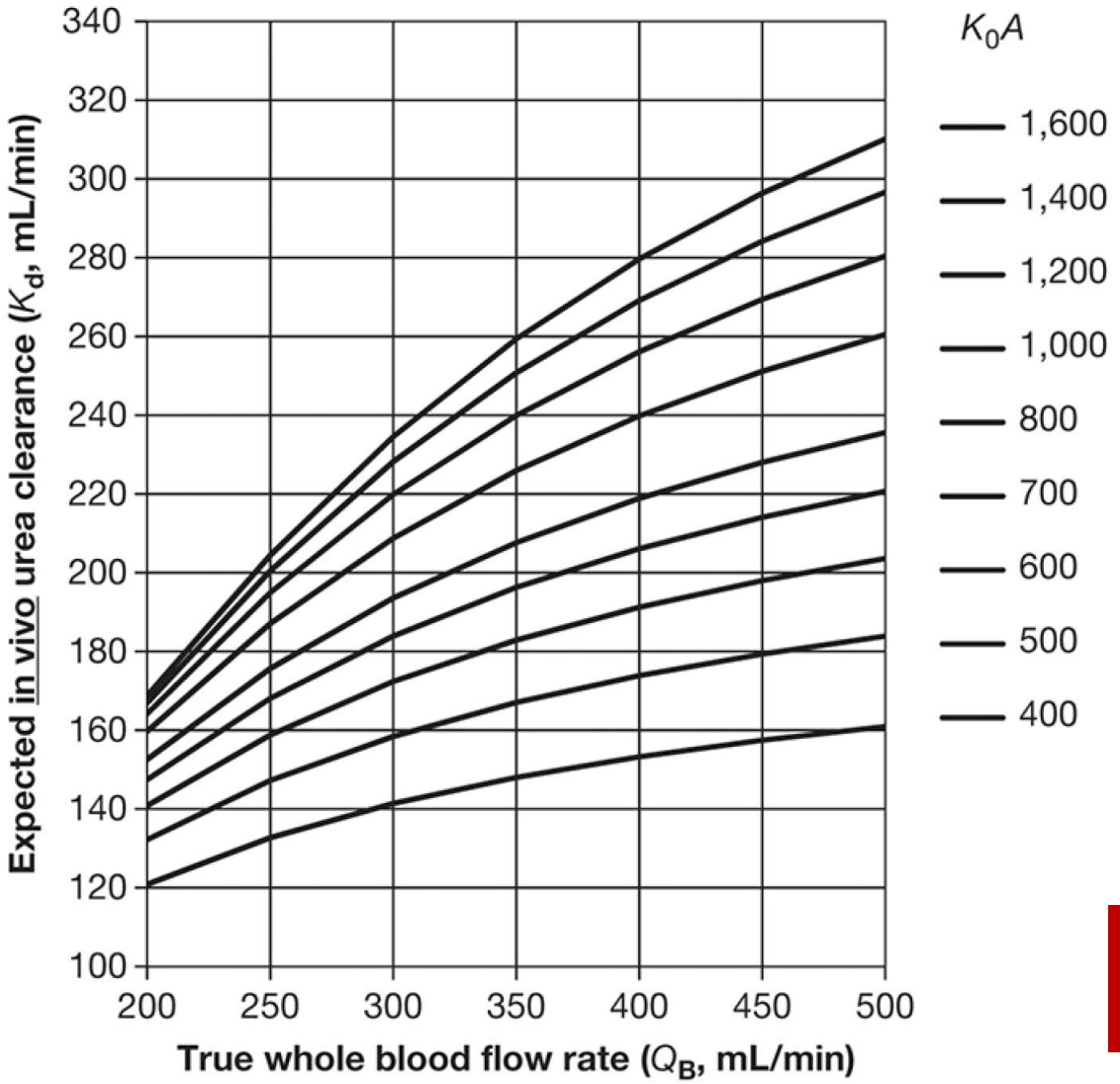
Thank you for your attention

Uremic toxin (updated) definition



Rosner MH, et al. Clin J Am Soc Nephrol. 2021 Dec;16(12):1918-1928.

Empirical calculation of spKt/V



Input
Sex & BW (for calculate V),
target Kt/V, session length, K_0A & BFR

⬇

We derive Kd (dialyzer urea clearance from graph)

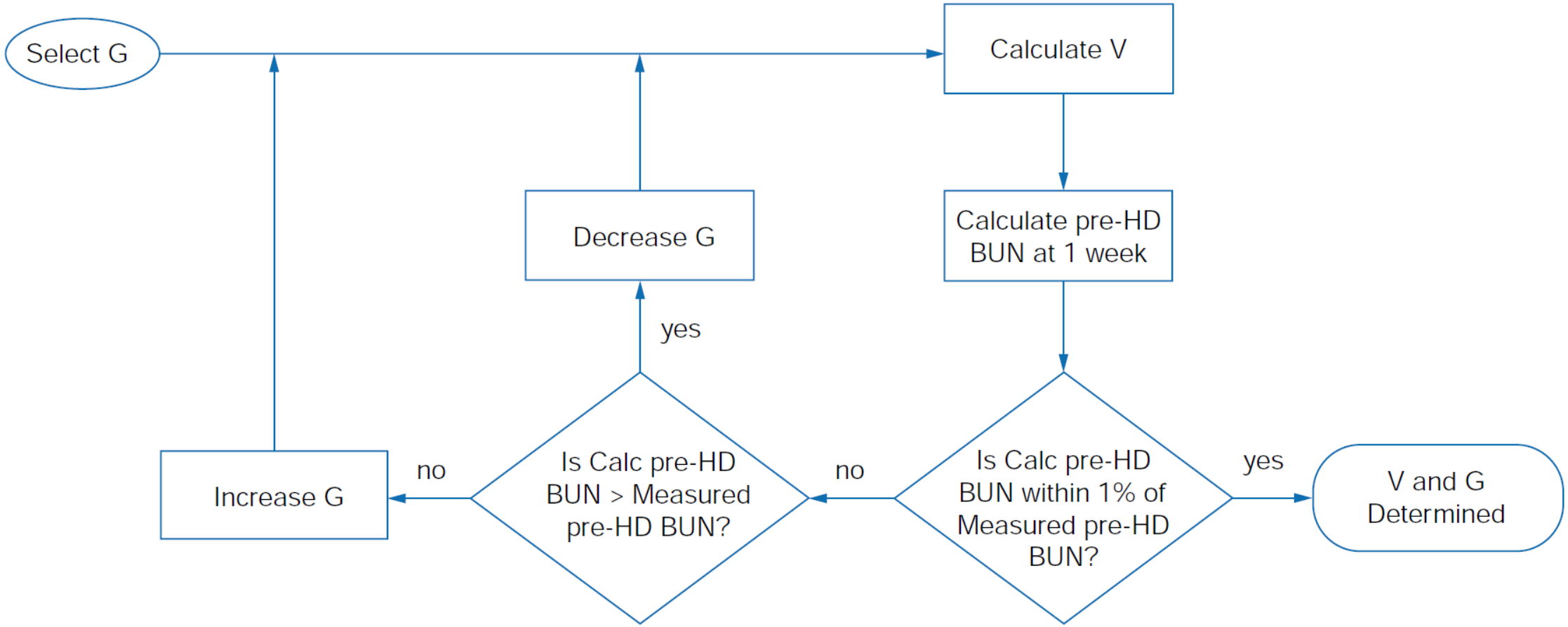
⬇

Kt/V

Empirical calculation should be avoided,
For not account to in vivo effect, no UF, no G, Reuse

Handbook of dialysis, 6th edition.

Computing formal urea kinetic model



G and Vurea can be computed from UKM (using pre & post-dialysis BUN), the program will plot models to calculate closest Pre-HD (within 1%) of measured pre-HD to select such V & G

Handbook of dialysis therapy, 6th edition.