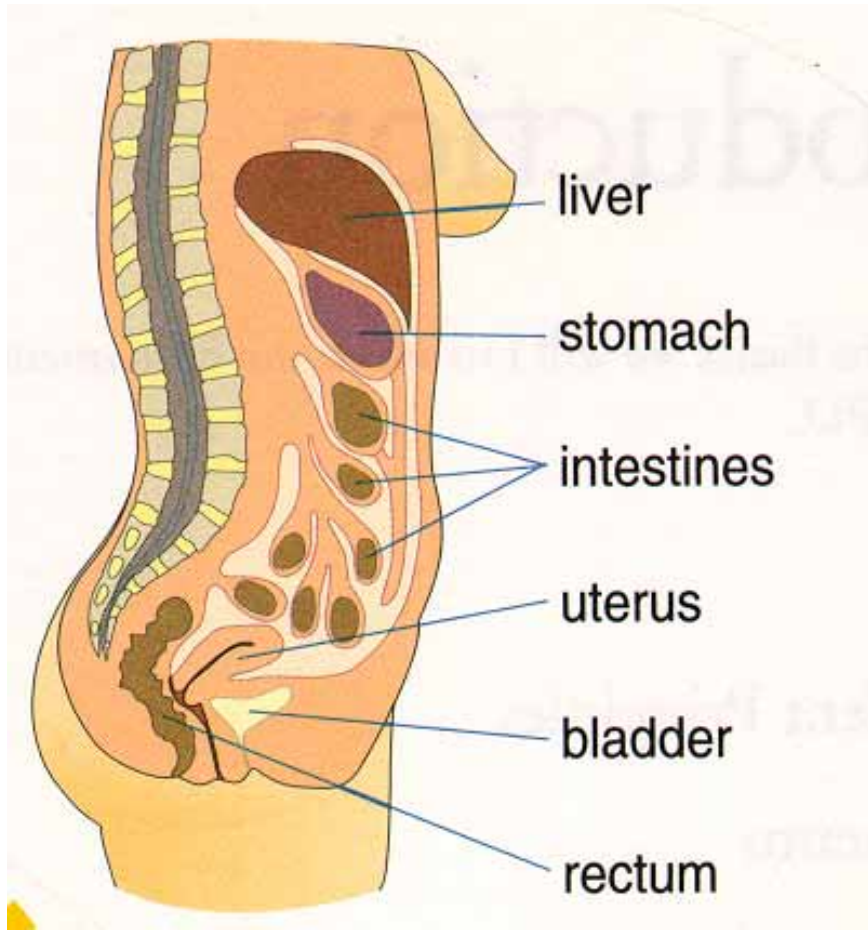
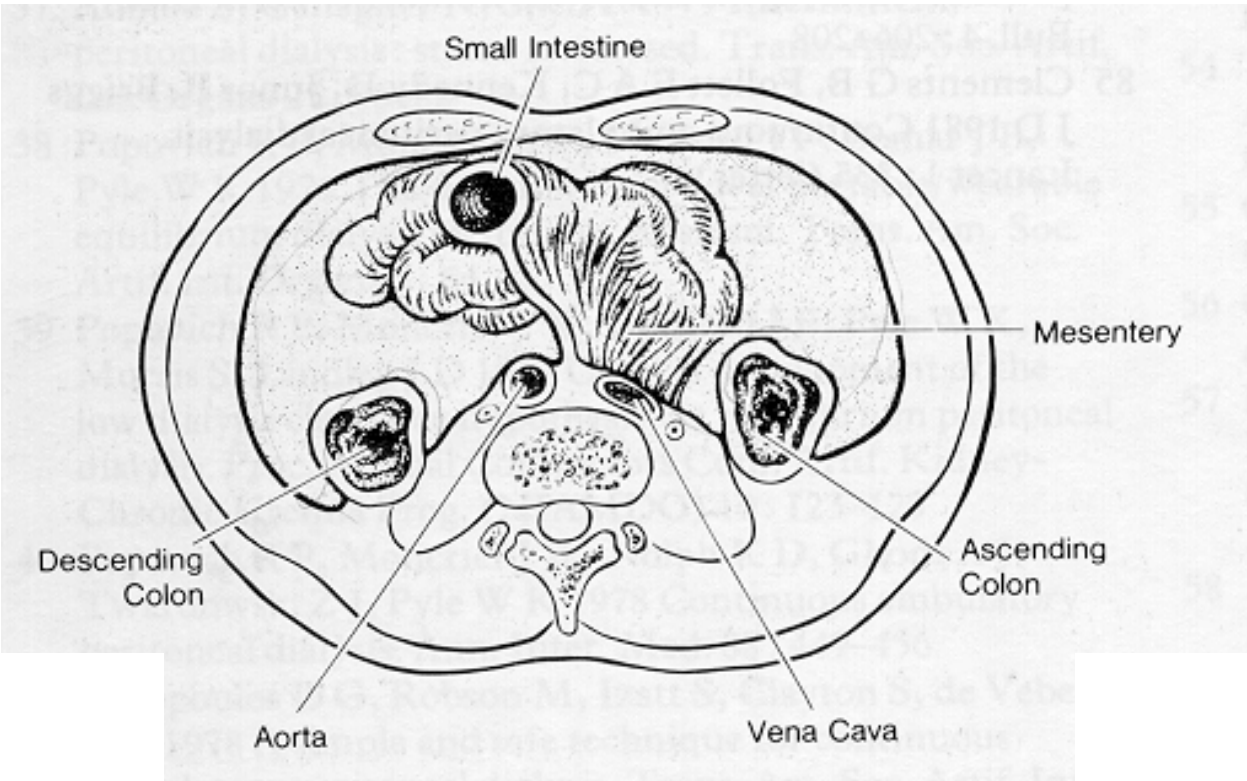
Peritoneal Anatomy

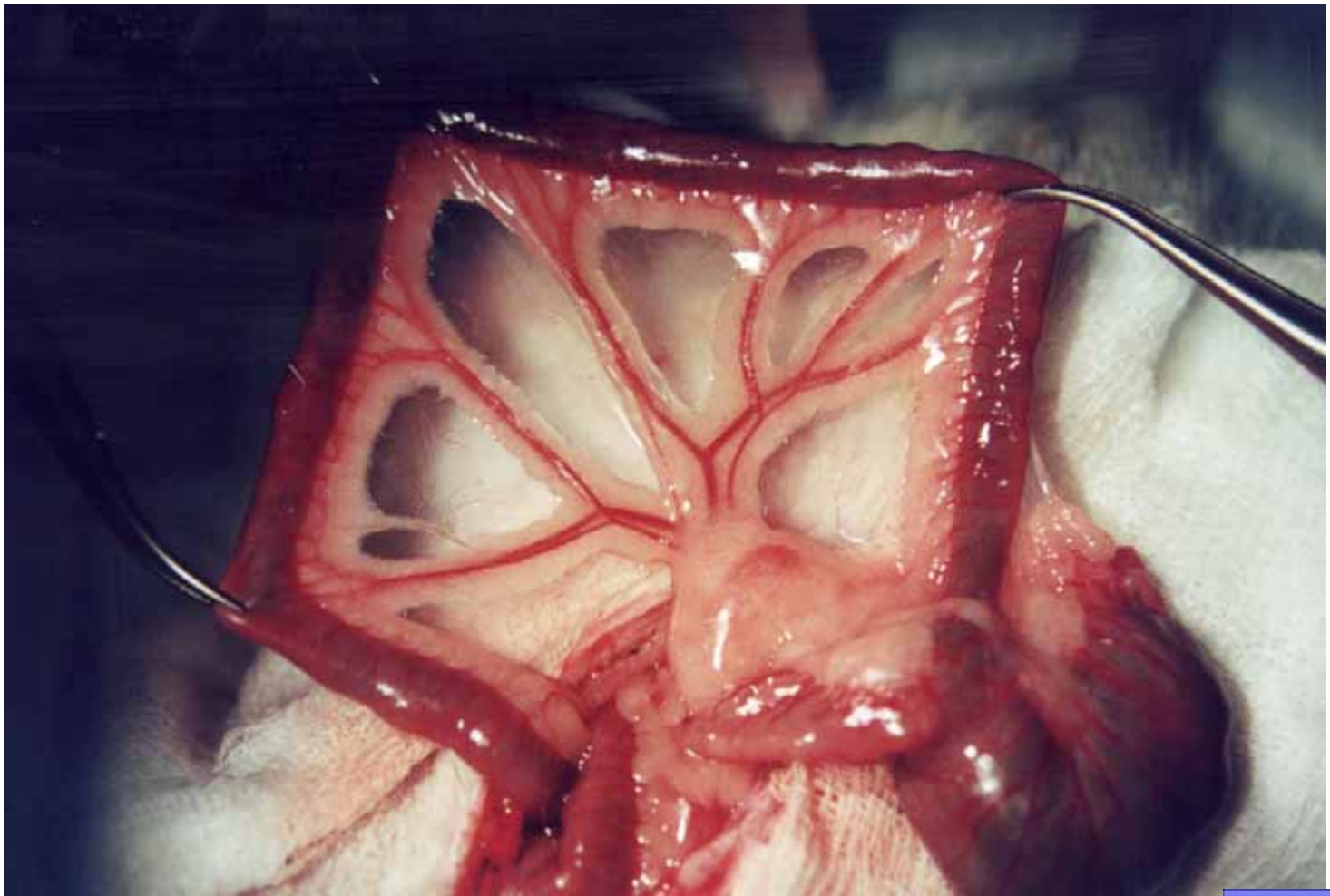
The peritoneum

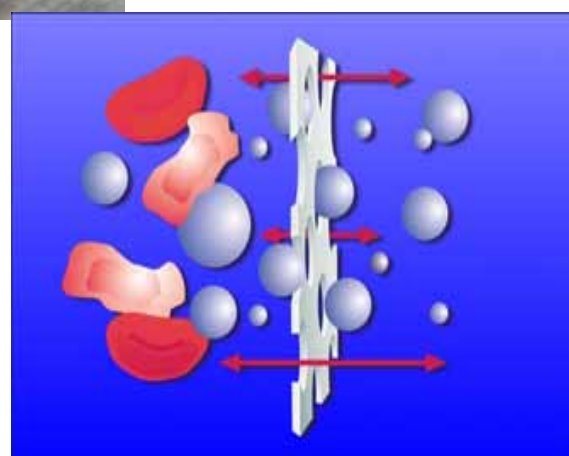


Peritoneal Anatomy

Cross section showing the peritoneal cavity and internal organs





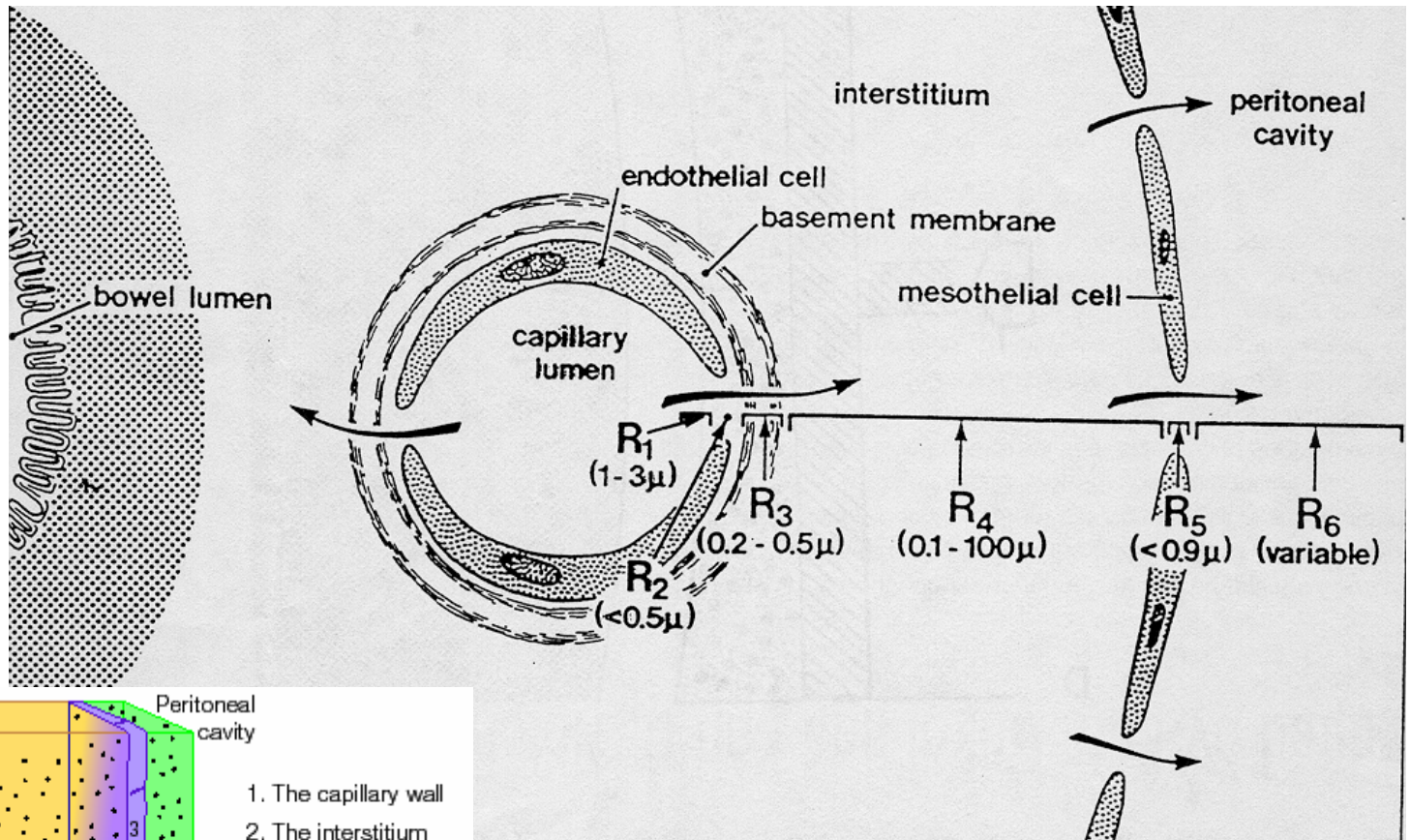


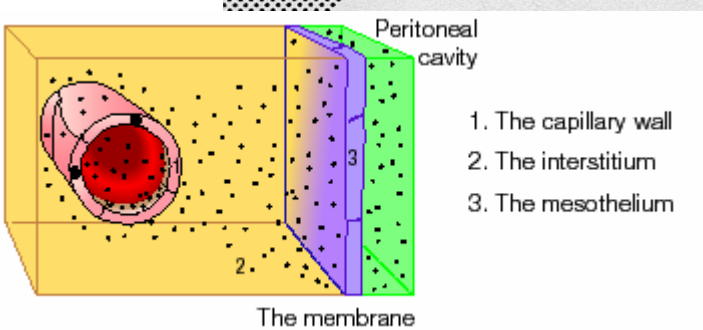
General principles

- **A liquid instilled in the peritoneal cavity will equilibrate with the composition of the blood compartment through:**
  - **DIFFUSION:** concentration gradient over a semi-permeable membrane
  - **CONVECTION:** "solute drag" by ultrafiltration.

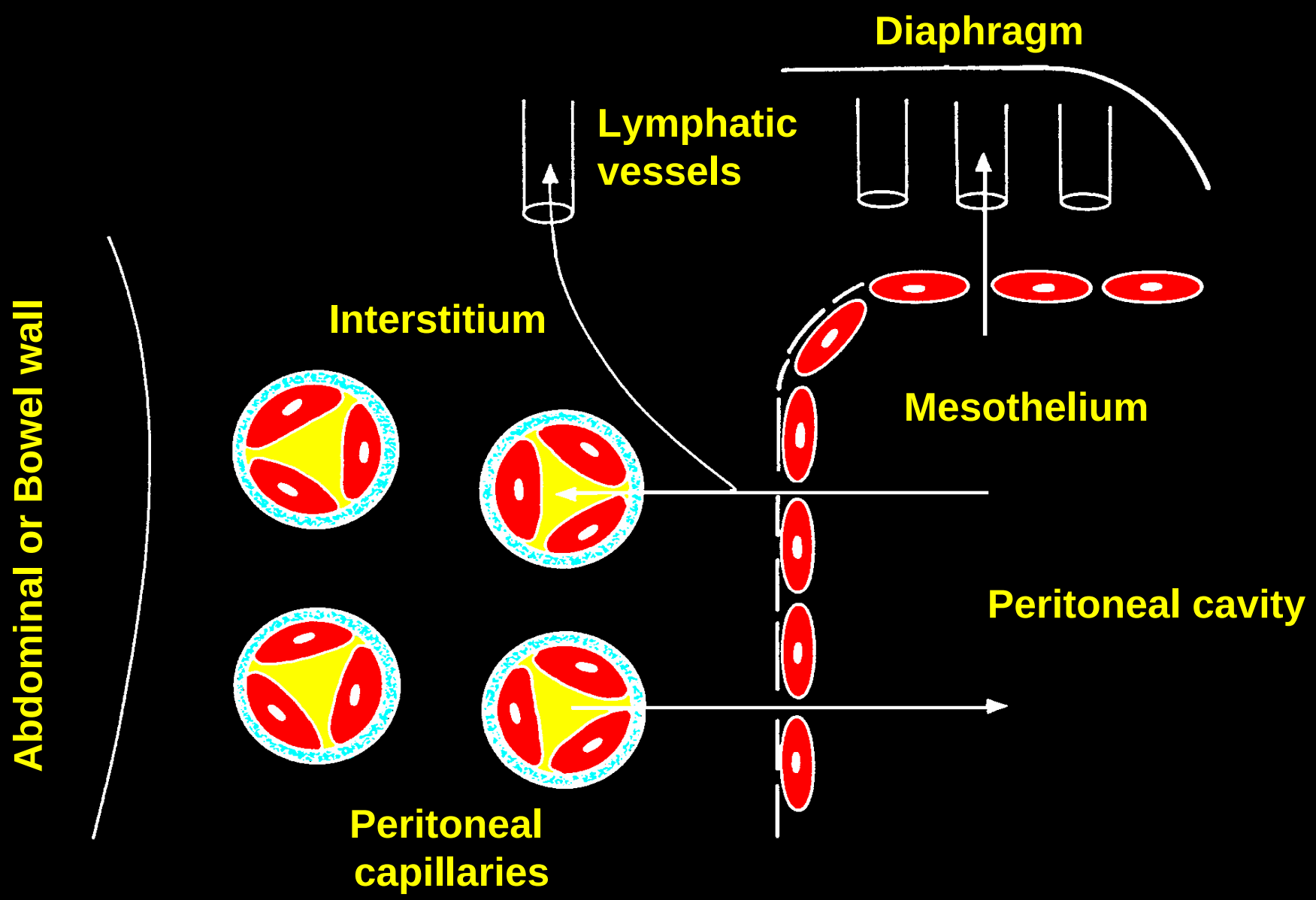
Peritoneal Physiology

Site of Resistance to Solute Movement



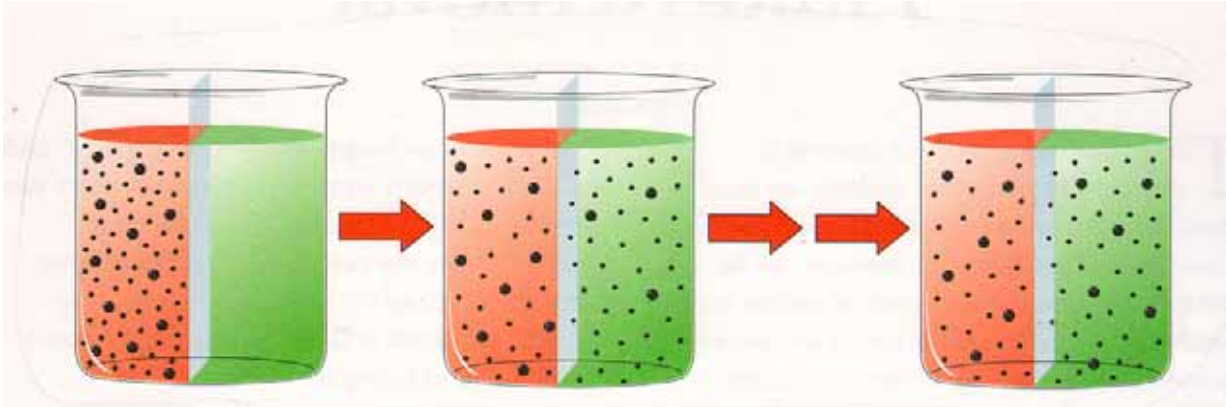


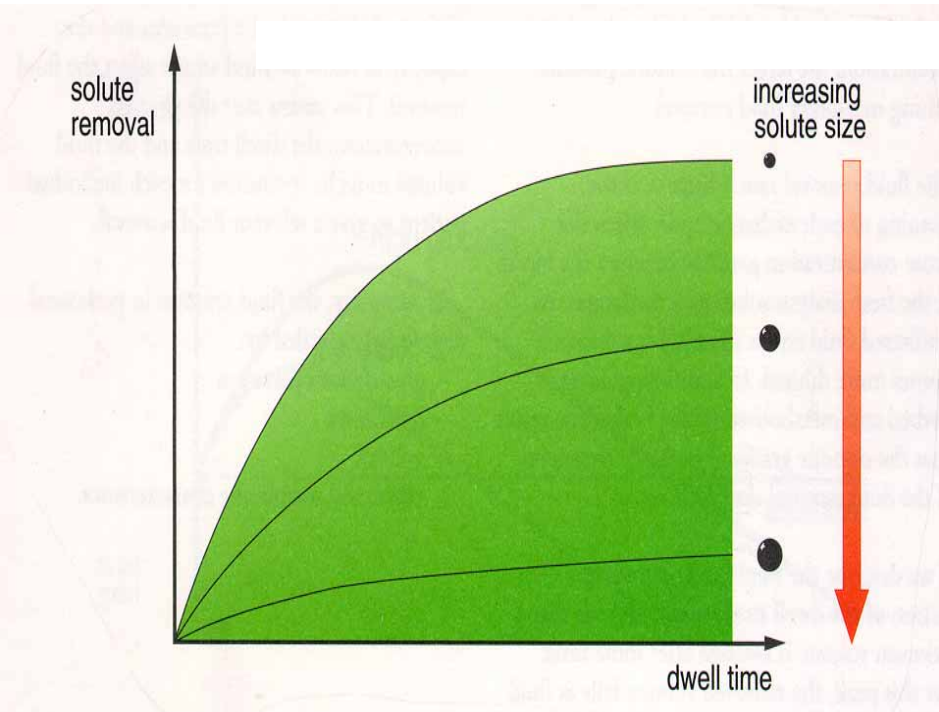
A schematic representation of the peritoneal membrane.



Peritoneal Physiology

Diffusion

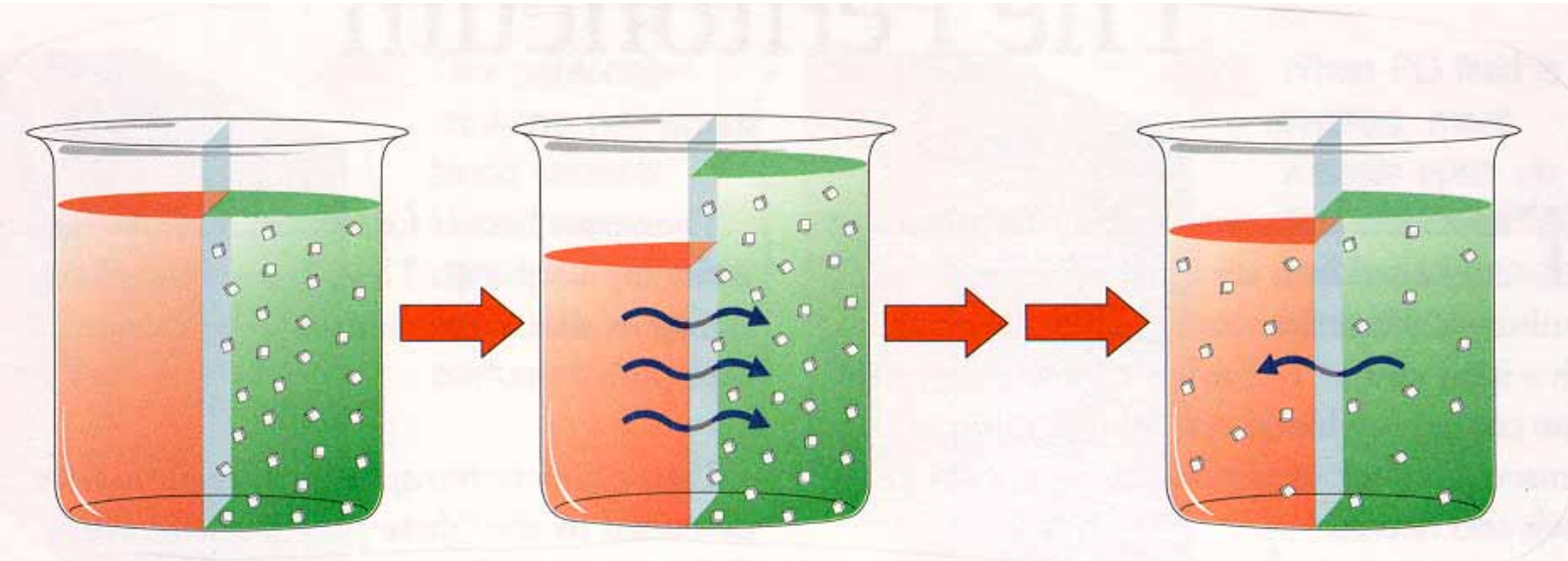




- concentrationgradient
- solute dimensions
- porosity of the membrane

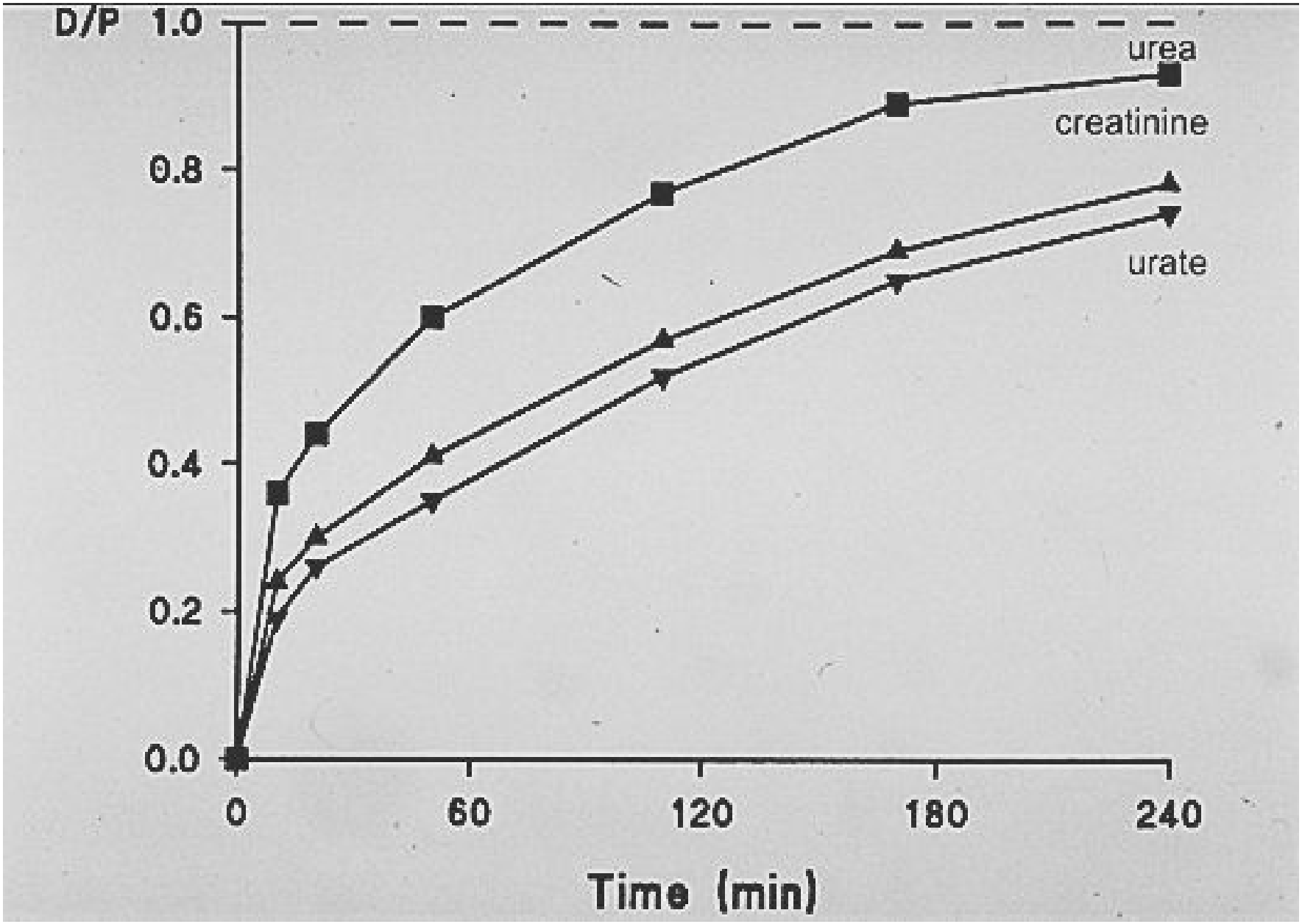
Peritoneal Physiology

Osmotic Ultrafiltration

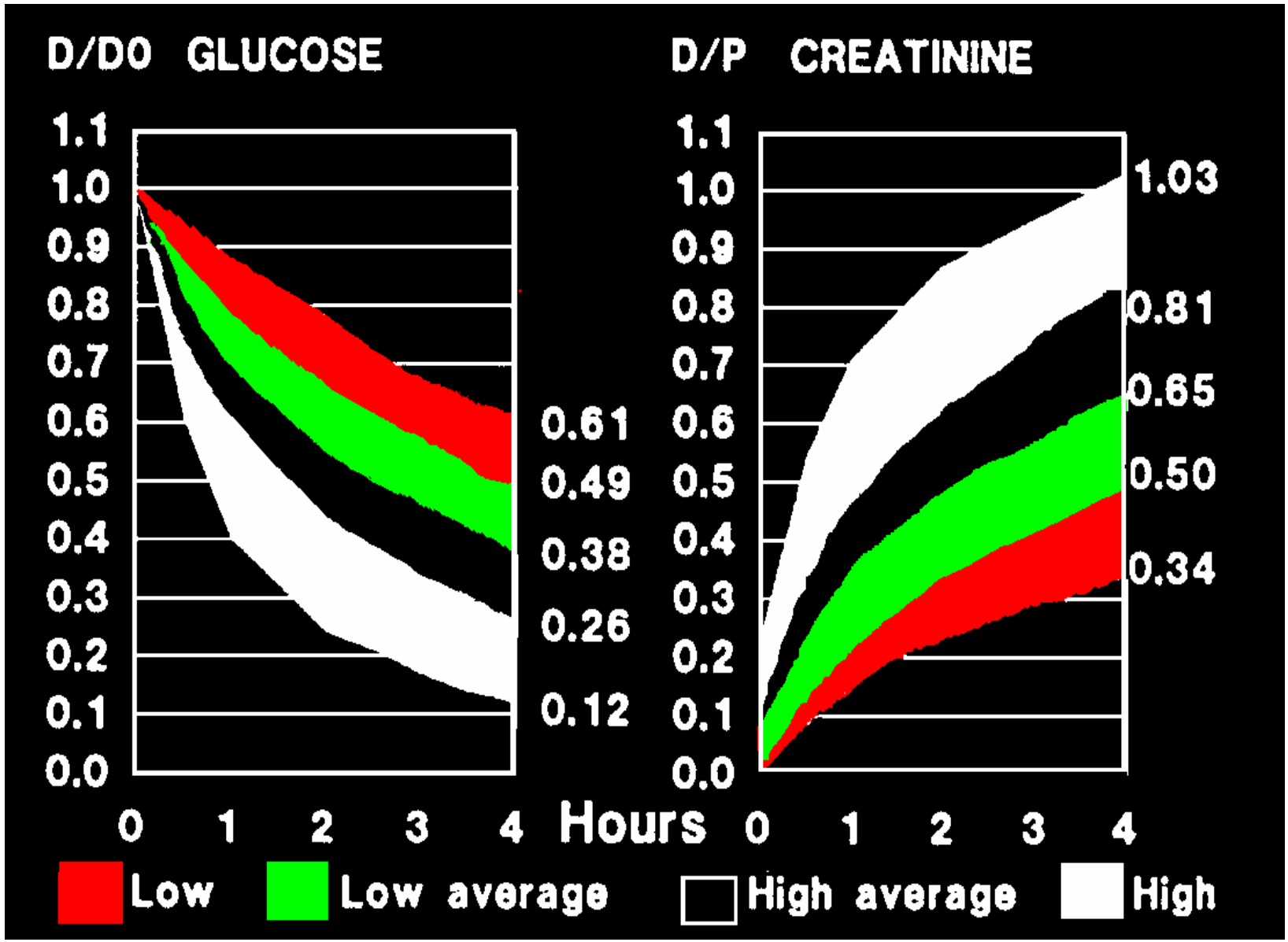


Convection and solute drag:

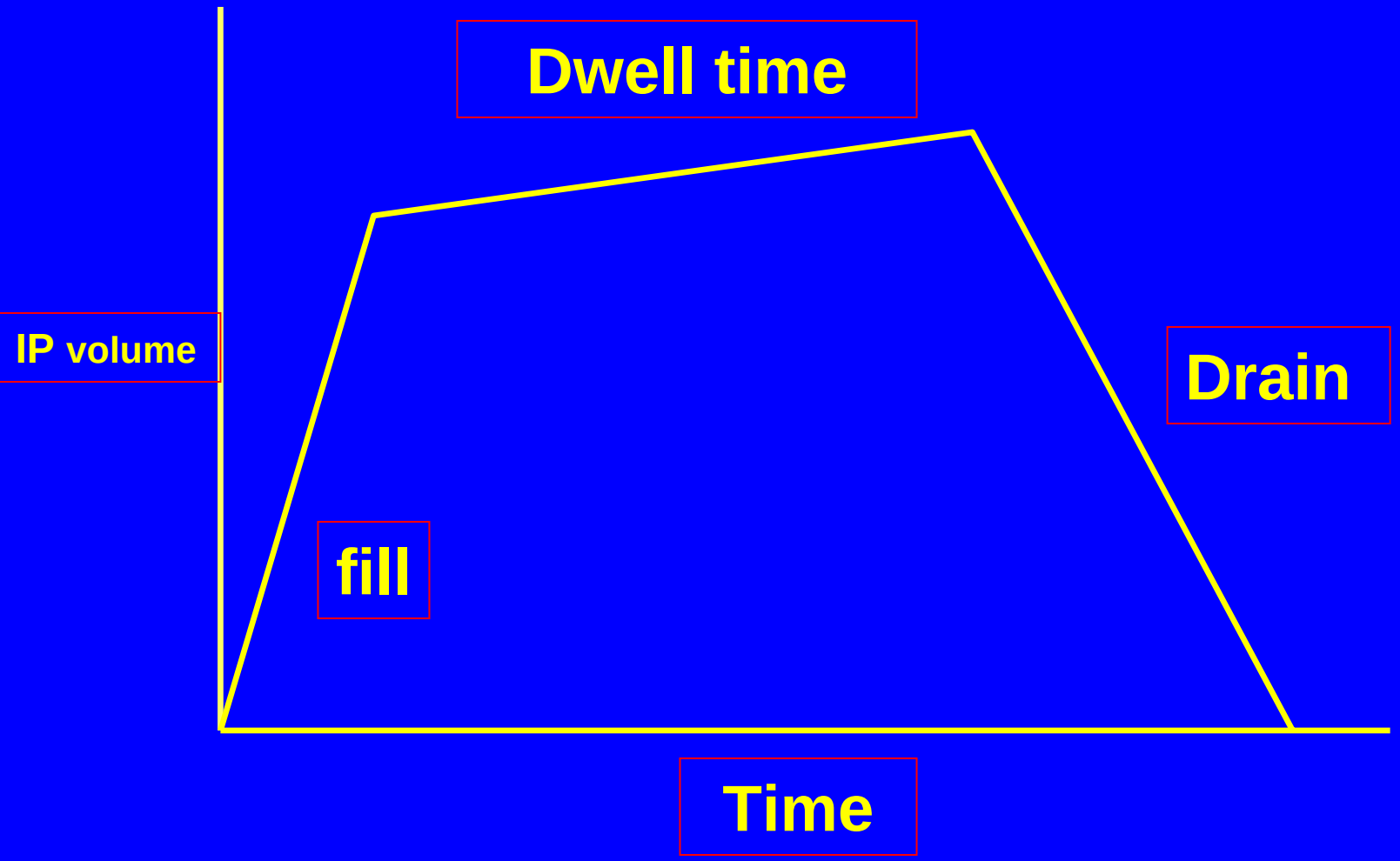
- **independent of solute size to cut off level**
- **Concentration (and not gradient) dependent**


D/P
1.0
0.8
0.6
0.4
0.2
0.0
urea
creatinine
urate
0
60
120
180
240
Time (min)

PET test.

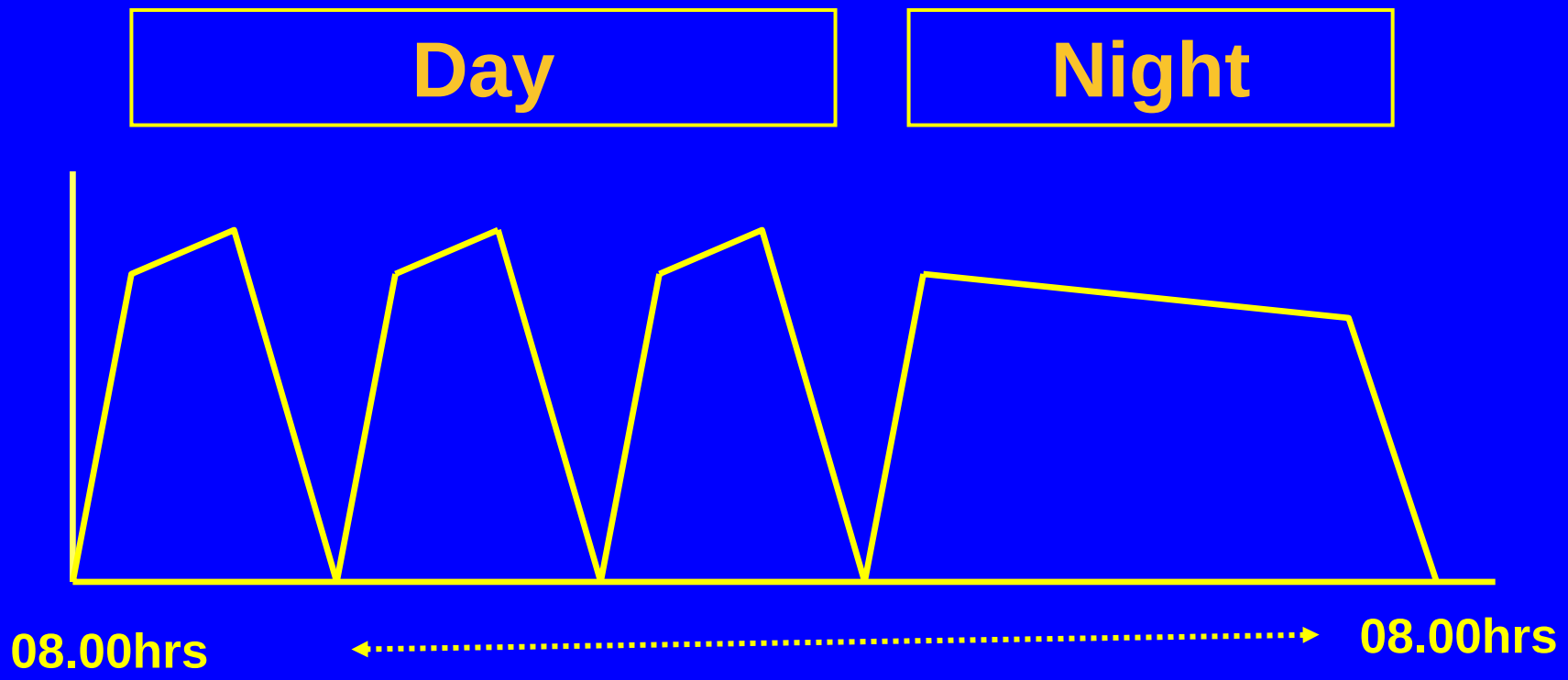

D/D0 GLUCOSE
D/P CREATININE
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.61
0.49
0.38
0.26
0.12
1.03
0.81
0.65
0.50
0.34
0 1 2 3 4 Hours 0 1 2 3 4
Low
Low average
High average
High

A PD dwell



CAPD – Classic dwell pattern

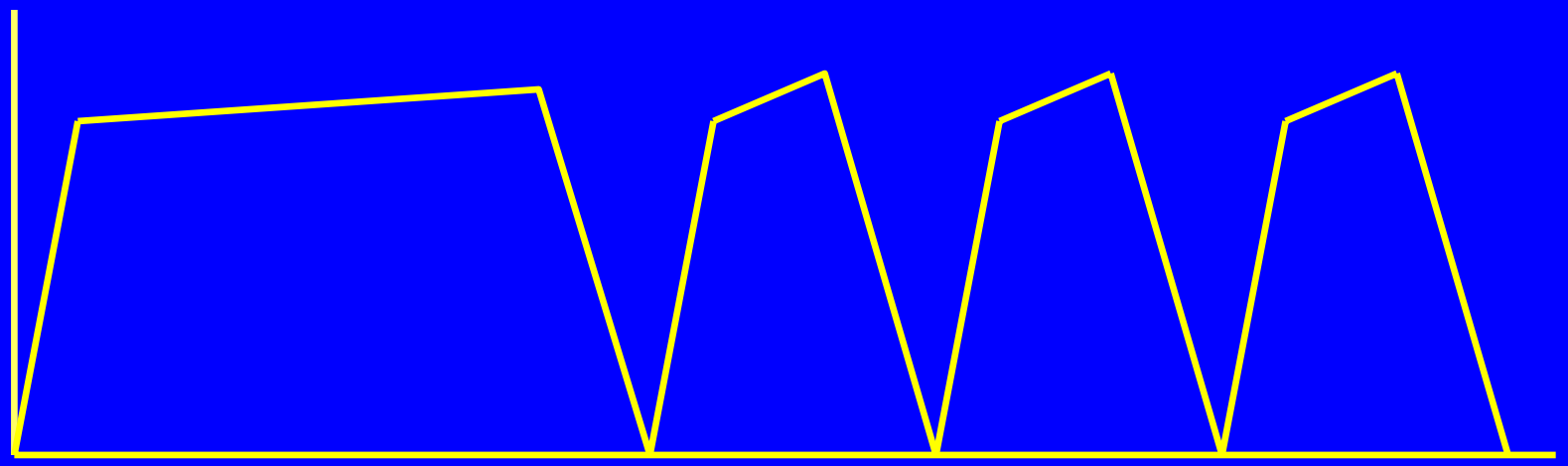
4 x 2000 or 4 x 2500 ml dialysate



APD – alternate CAPD

Day

Night



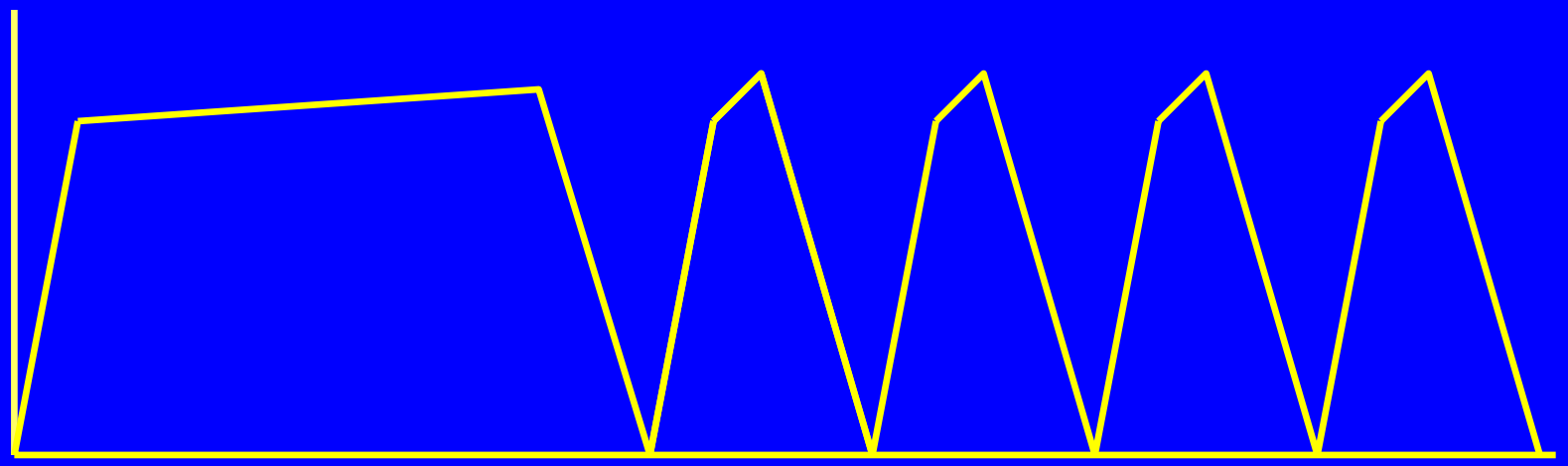
08.00hrs

08.00hrs

APD – low volume

Day

Night



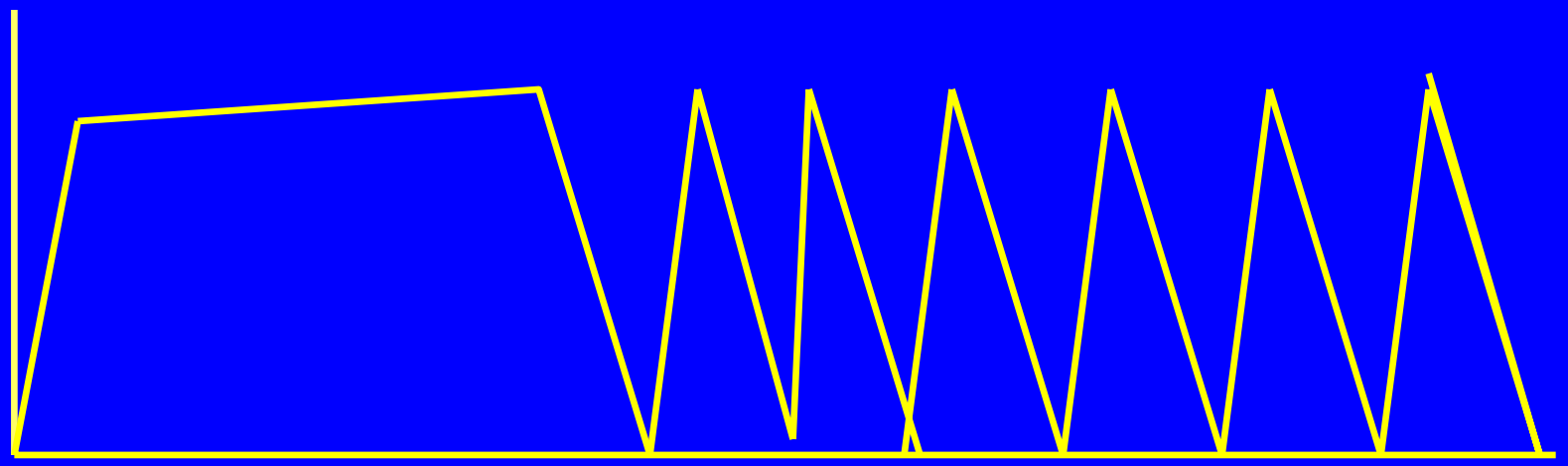
08.00hrs

08.00hrs

APD – high volume CCPD

Day

Night



08.00hrs

08.00hrs

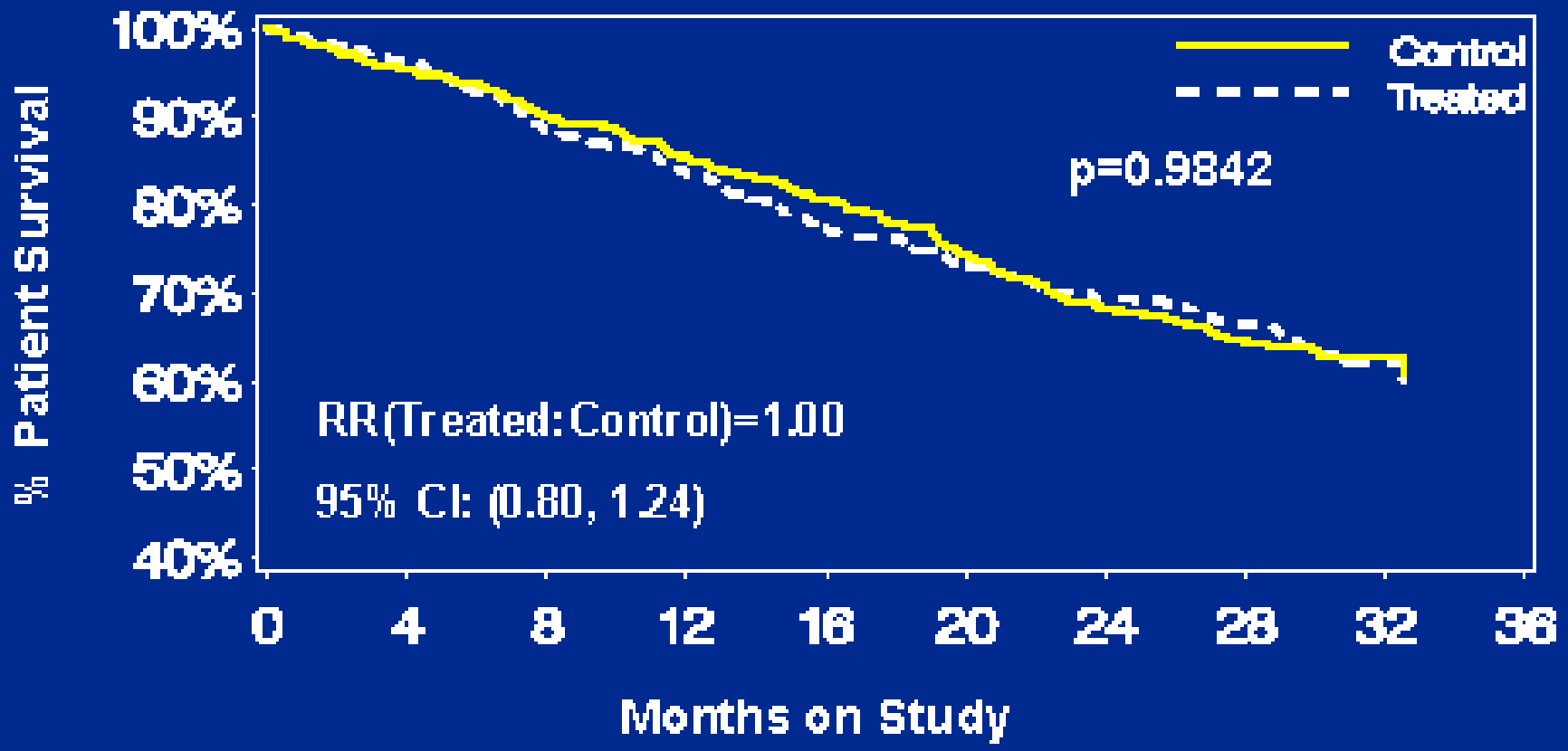
More is not always better!

ADEMEX: Primary Outcome

ITT Patient Survival Comparing Treatment Groups

Log–rank Test: Chi–square = 0.0004, p–value 0.9842

(Control Group: Events/No. Pts = 157/484, Treatment Group: Events/No. Pts = 153/481)

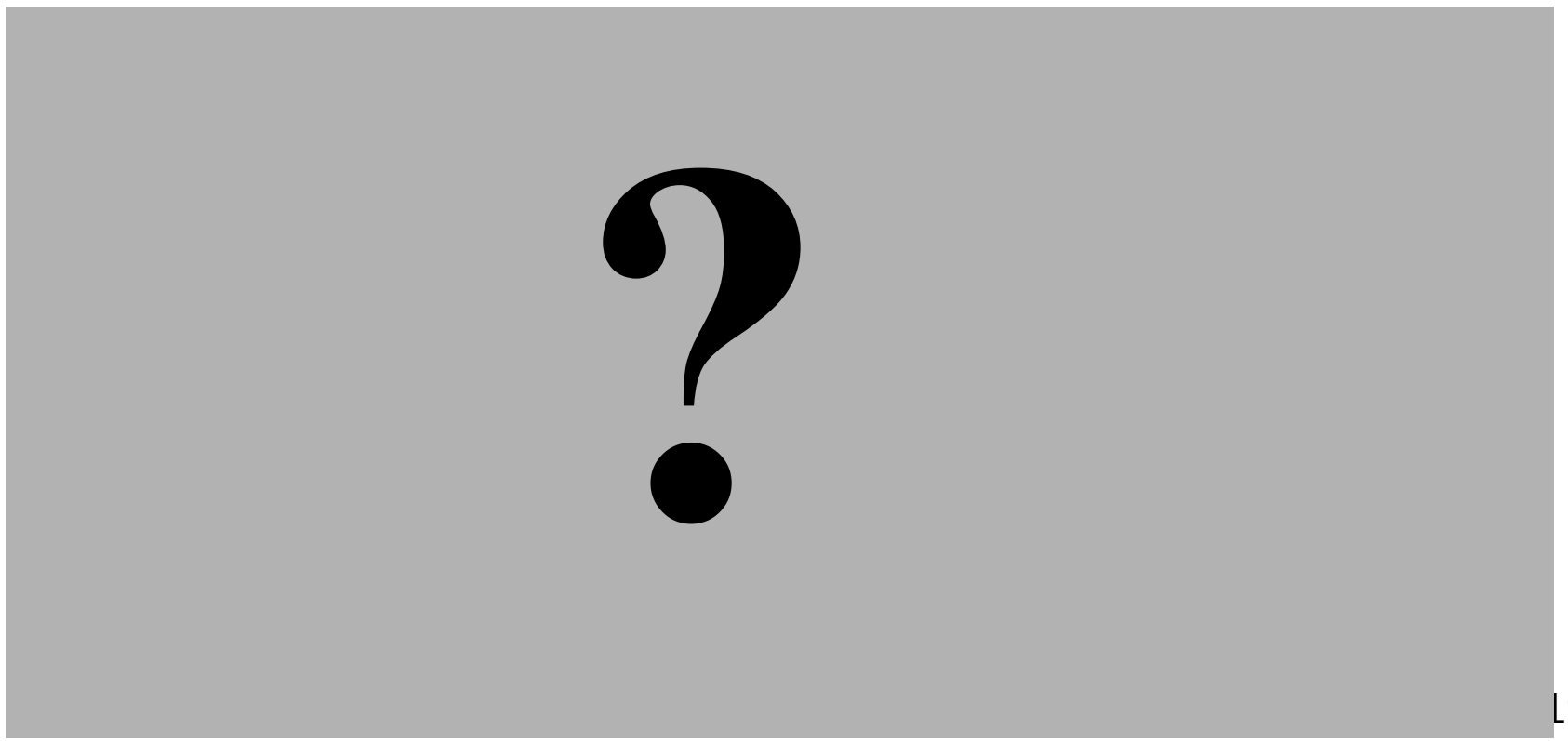


Efficient use of solution in APD.

BSA 1.71 - 2.0m²
RRF = 0 mL

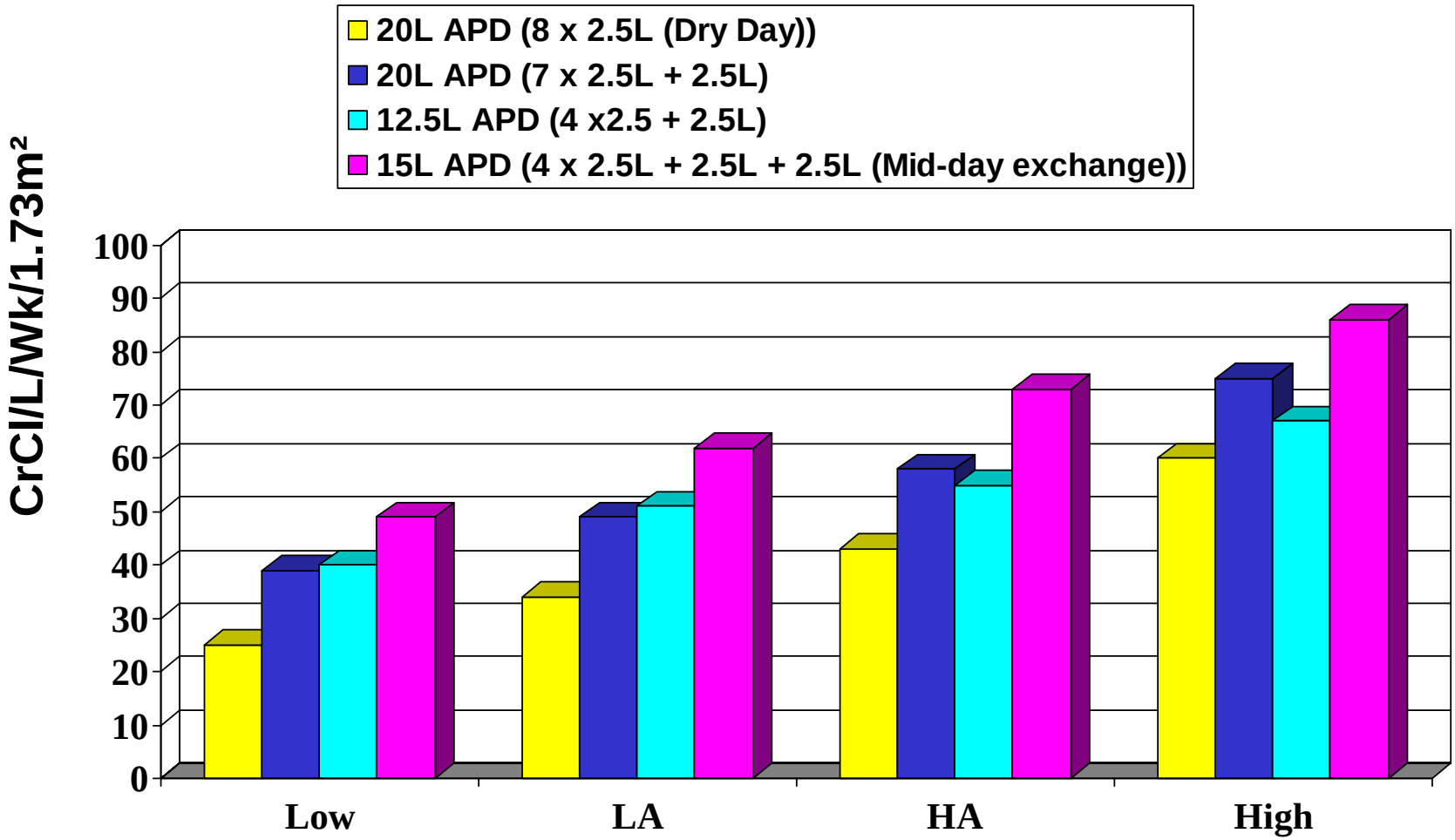
- 20L APD (8 x 2.5L (Dry Day))
- 20L APD (7 x 2.5L + 2.5L)
- 12.5L APD (4 x2.5 + 2.5L)
- 15L APD (4 x 2.5L + 2.5L + 2.5L (Mid-day exchange))

CrCl/L/Wk/1.73m²



Efficient use of solution in APD.

BSA 1.71 - 2.0m²
RRF = 0 mL



Blake et al, PDI, 16, 199

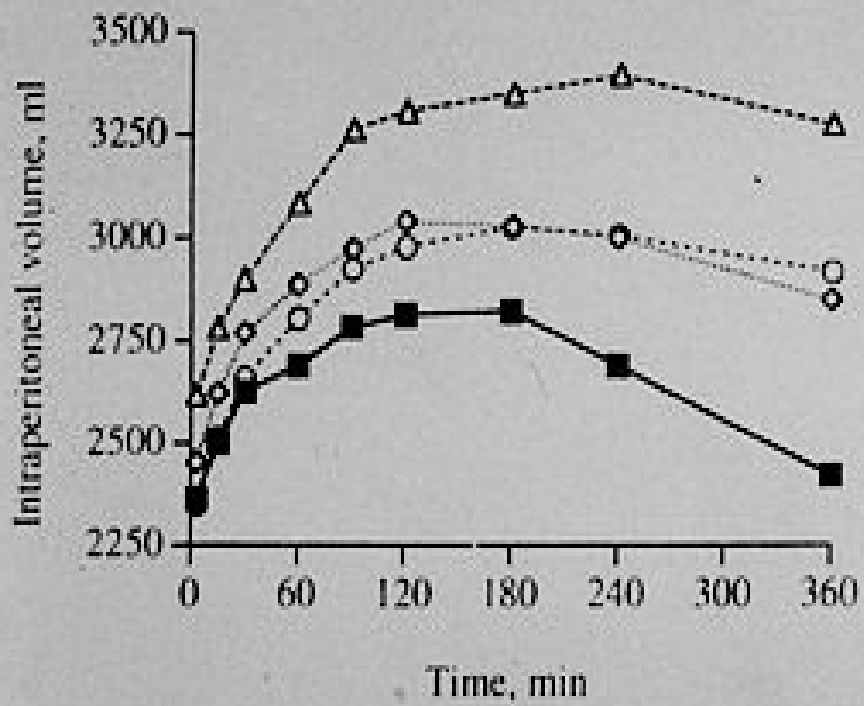
Quantified measurement of adequacy

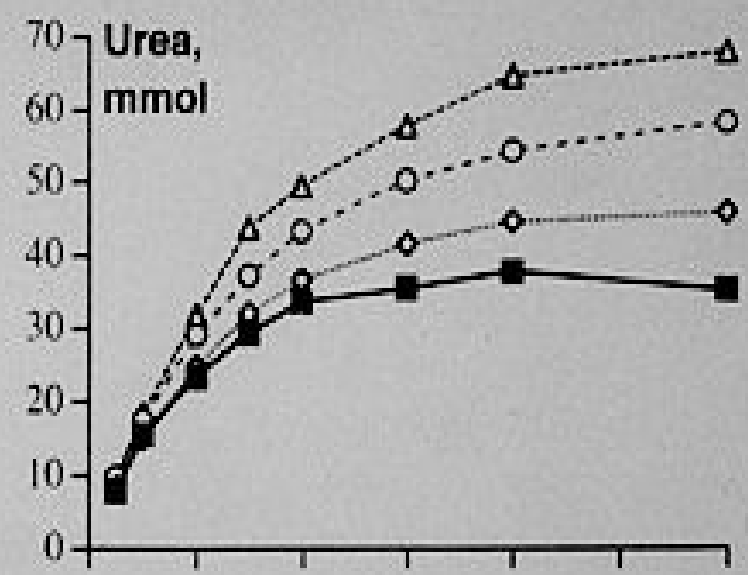
Urea kinetic modelling:

1) Kt/V: sum of the peritonal clearance of urea and the residual renal urea clearance, multiplied by 24 hours and divided by the volume of distribution.

$$\text{Kt/V renal} = \frac{\text{Total urinary volume} * \text{urinary urea concentration}}{\text{plasma urea concentration} * V}$$

$$\text{Kt/V}_{\text{peritoneal}} = \frac{\text{Total dialysate volume} * \text{dialysate urea concentration}}{\text{plasma urea concentration} * V}$$





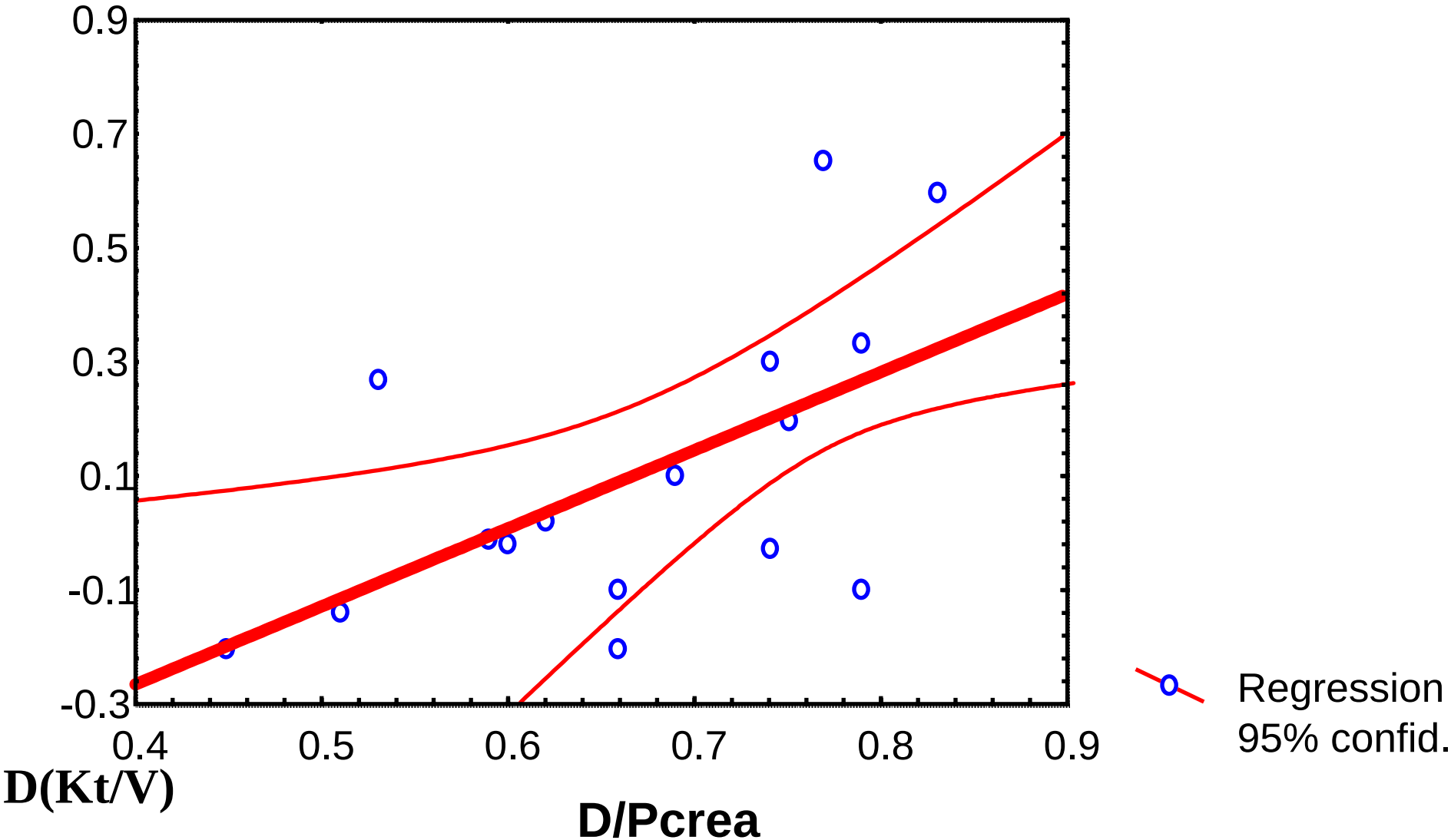
■ high transport (n = 7) ◊ high average (n = 20)
○ low average (n = 13) Δ low transport (n = 6)

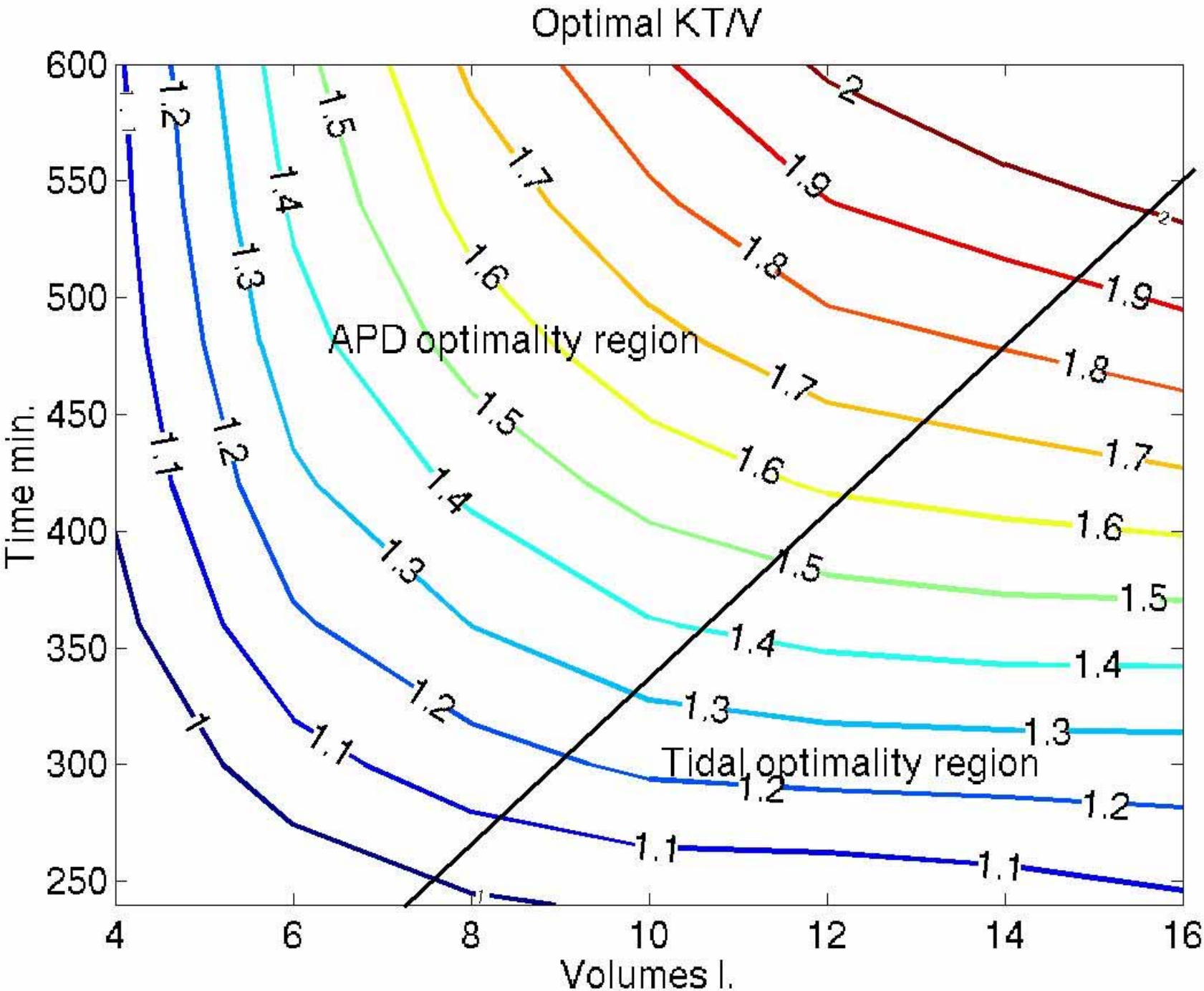
From: Wang et al. Nephrol Dial Transplant, 1998

Simulated CCPD versus CAPD

Delta Kt/V = -.8132 + 1.3696 * D/P

Correlation: r = .58006



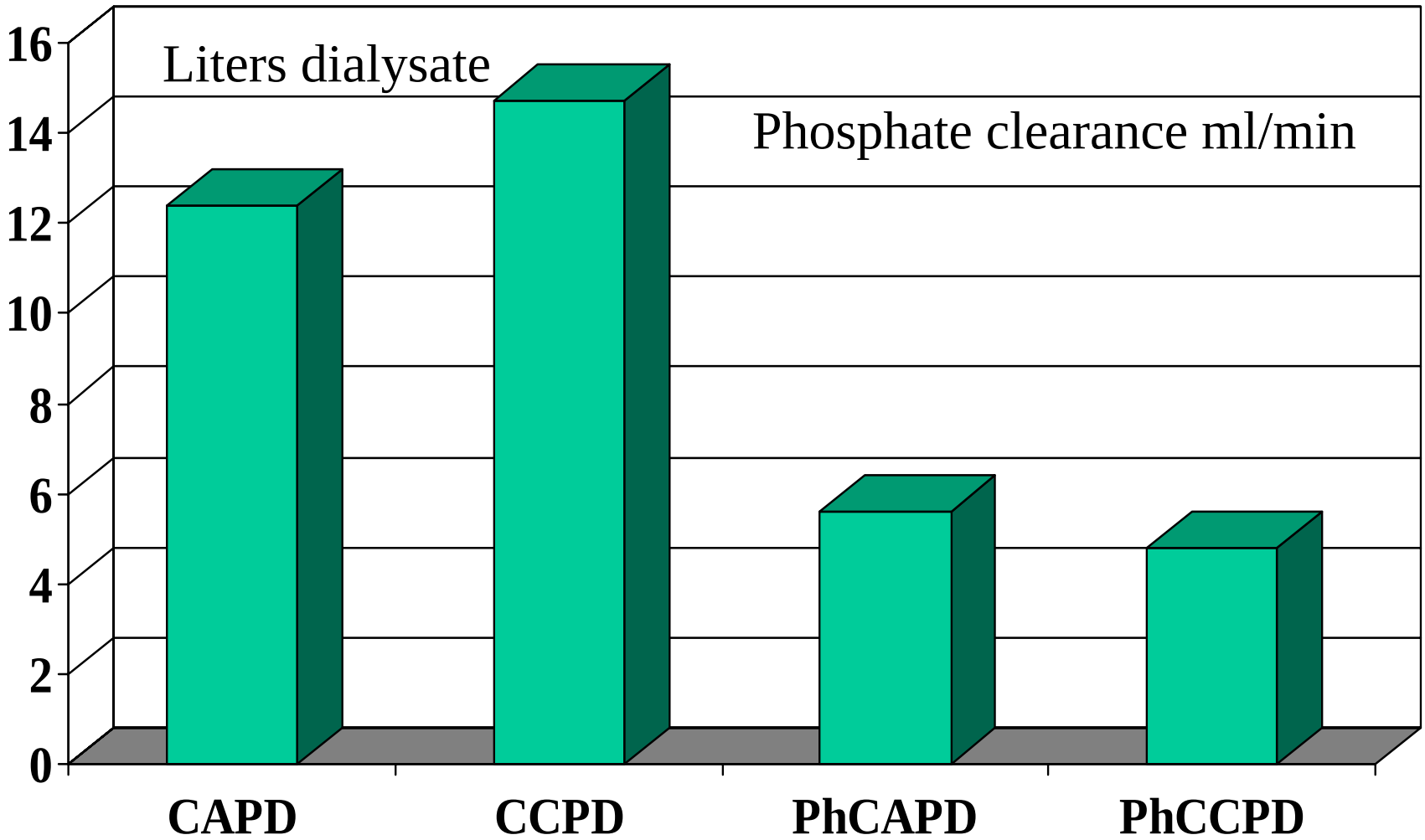

Optimal KT/V
Time min.
Volumes l.
APD optimality region
Tidal optimality region
600
550
500
450
400
350
300
250
4
6
8
10
12
14
16
1
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2

Quantified measurement of adequacy

Ratio's of D/P for creatinine and urea

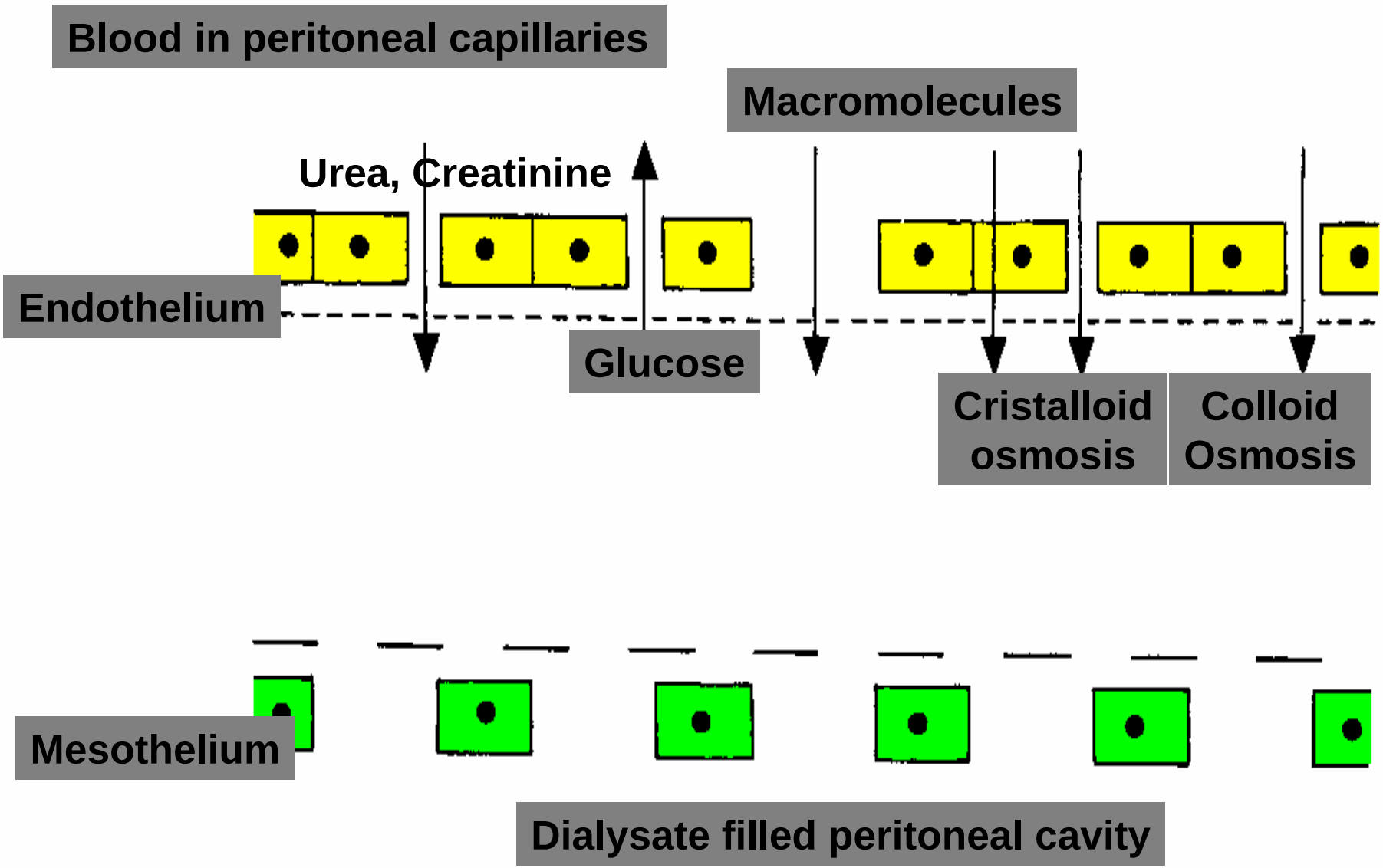
Dwell-time (hrs)	1	3	6
Low transporter	0.48	0.50	0.57
Low average transporter	0.57	0.62	0.70
High average transporter	0.68	0.74	0.82
High transporter	0.79	0.87	0.93

Phosphate clearance in CAPDvs CCPD

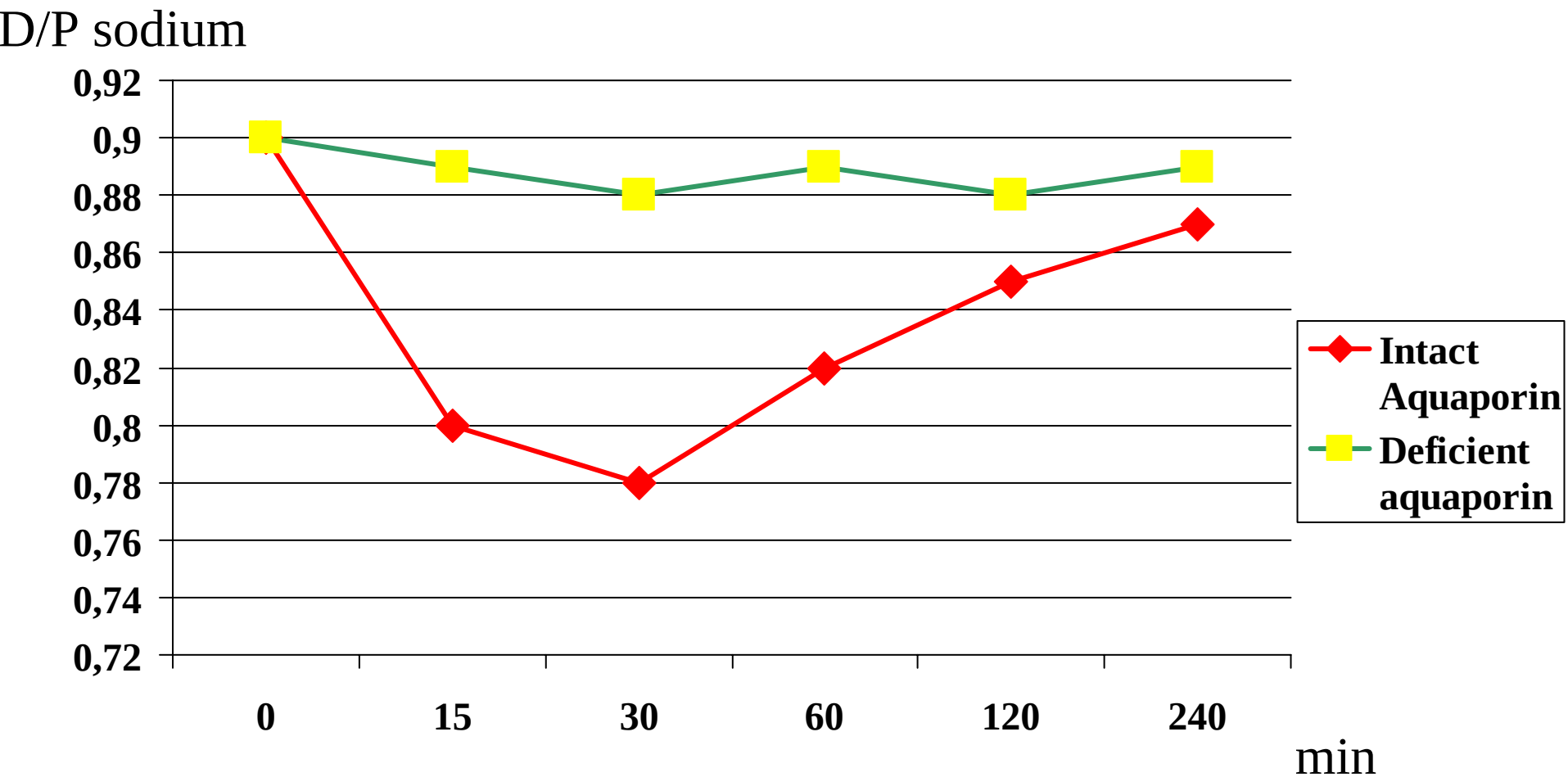


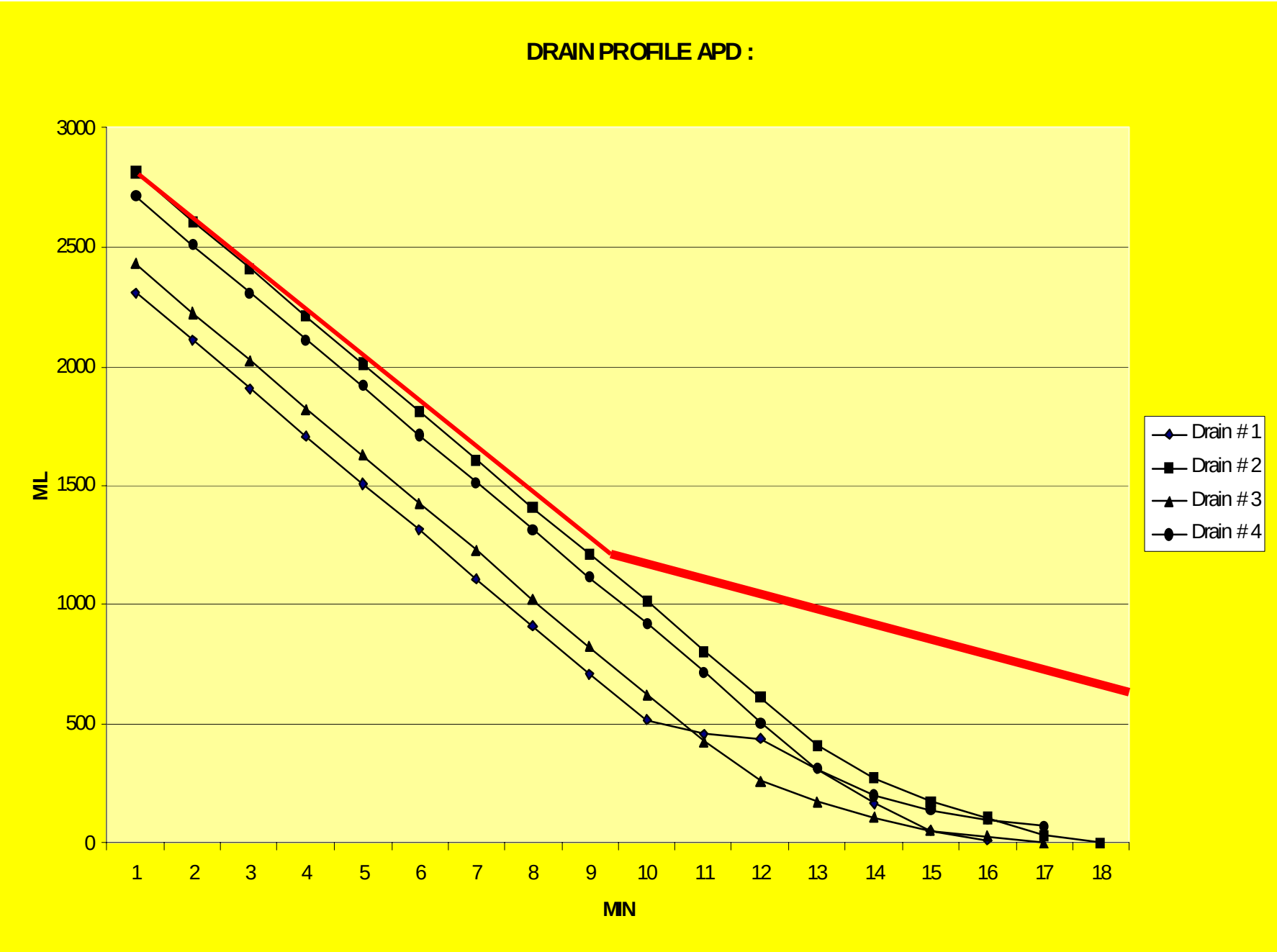
Sedlacek et al, AJKD 2000, 36, 1020-1024

The three-pore model and ultrafiltration

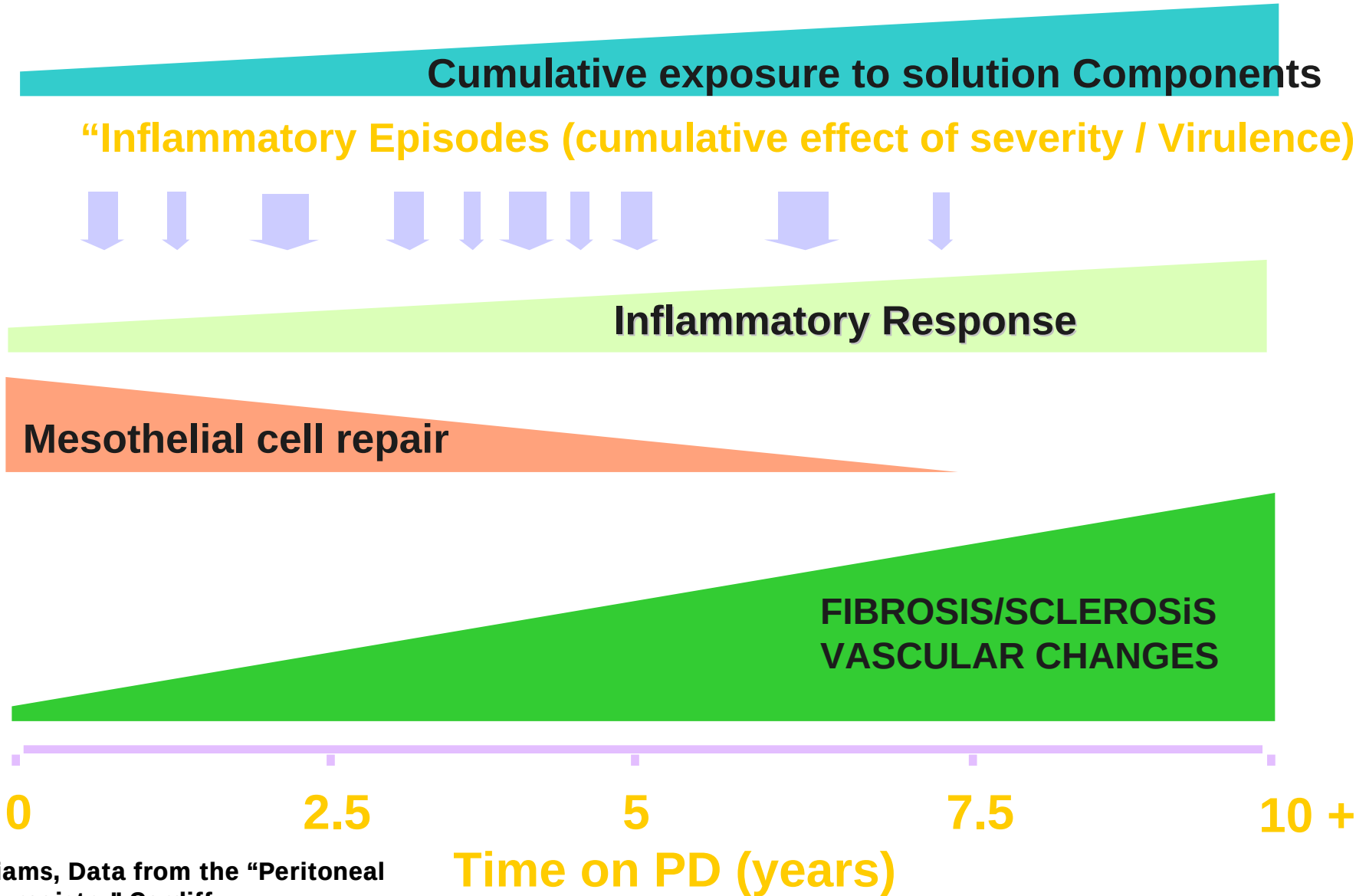


Modified PET: Sodium sieving and D/P sodium



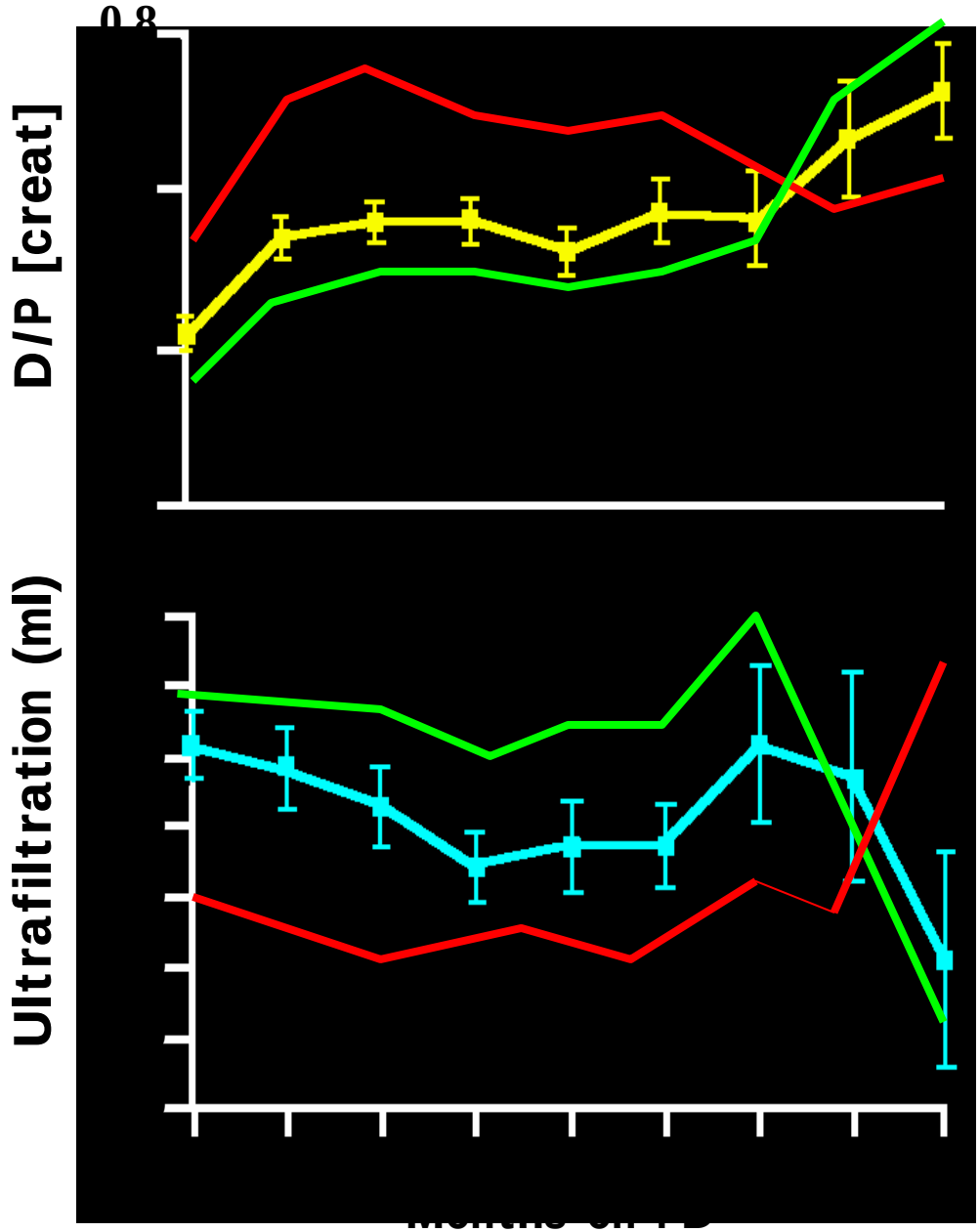

DRAIN PROFILE APD :
3000
2500
2000
1500
1000
500
0
ML
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
MIN
Drain # 1
Drain # 2
Drain # 3
Drain # 4

Changes in the peritoneum during PD



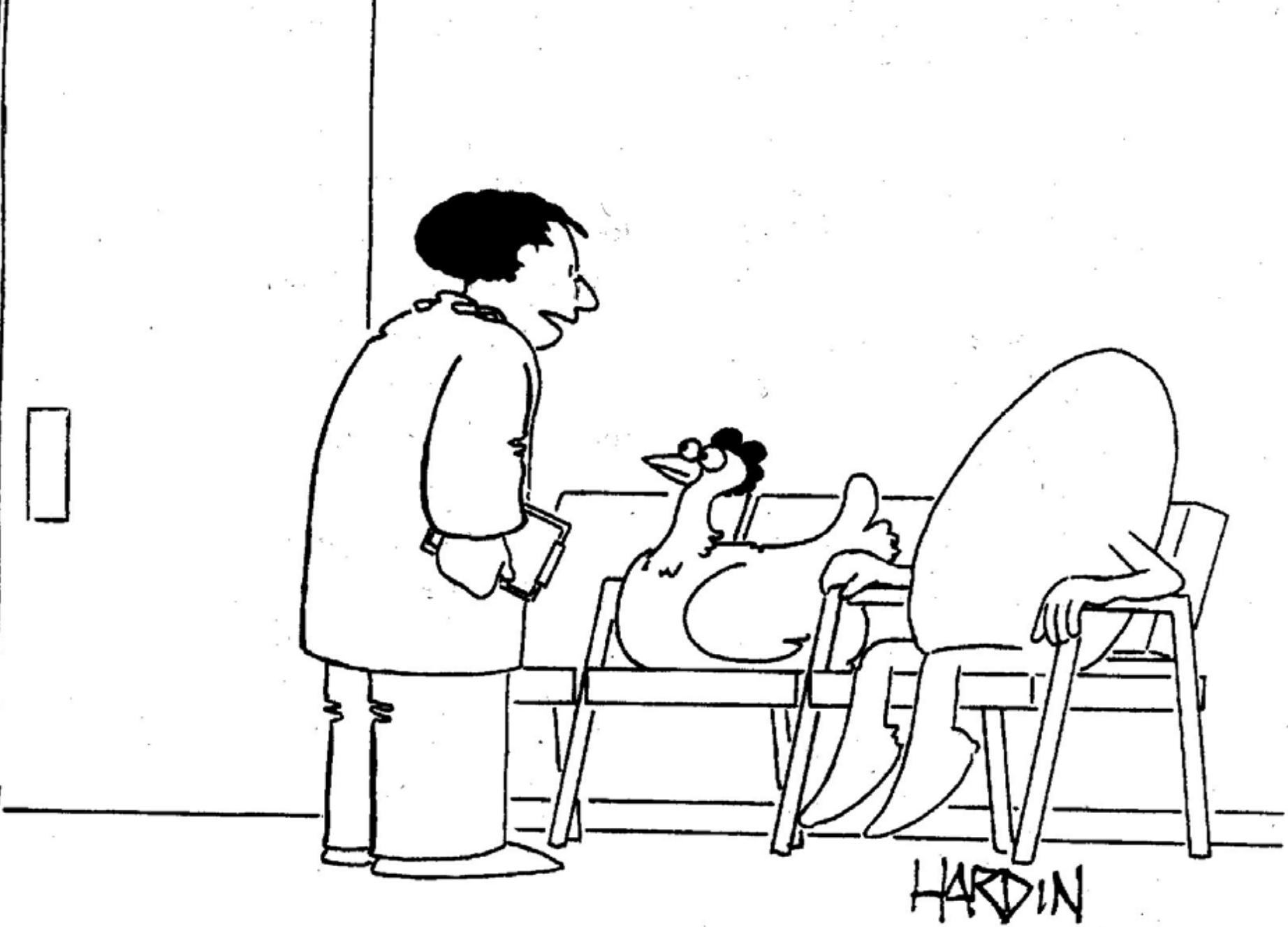
Williams, Data from the “Peritoneal biopsy registry” Cardiff

Long-term PD : Functional Changes.



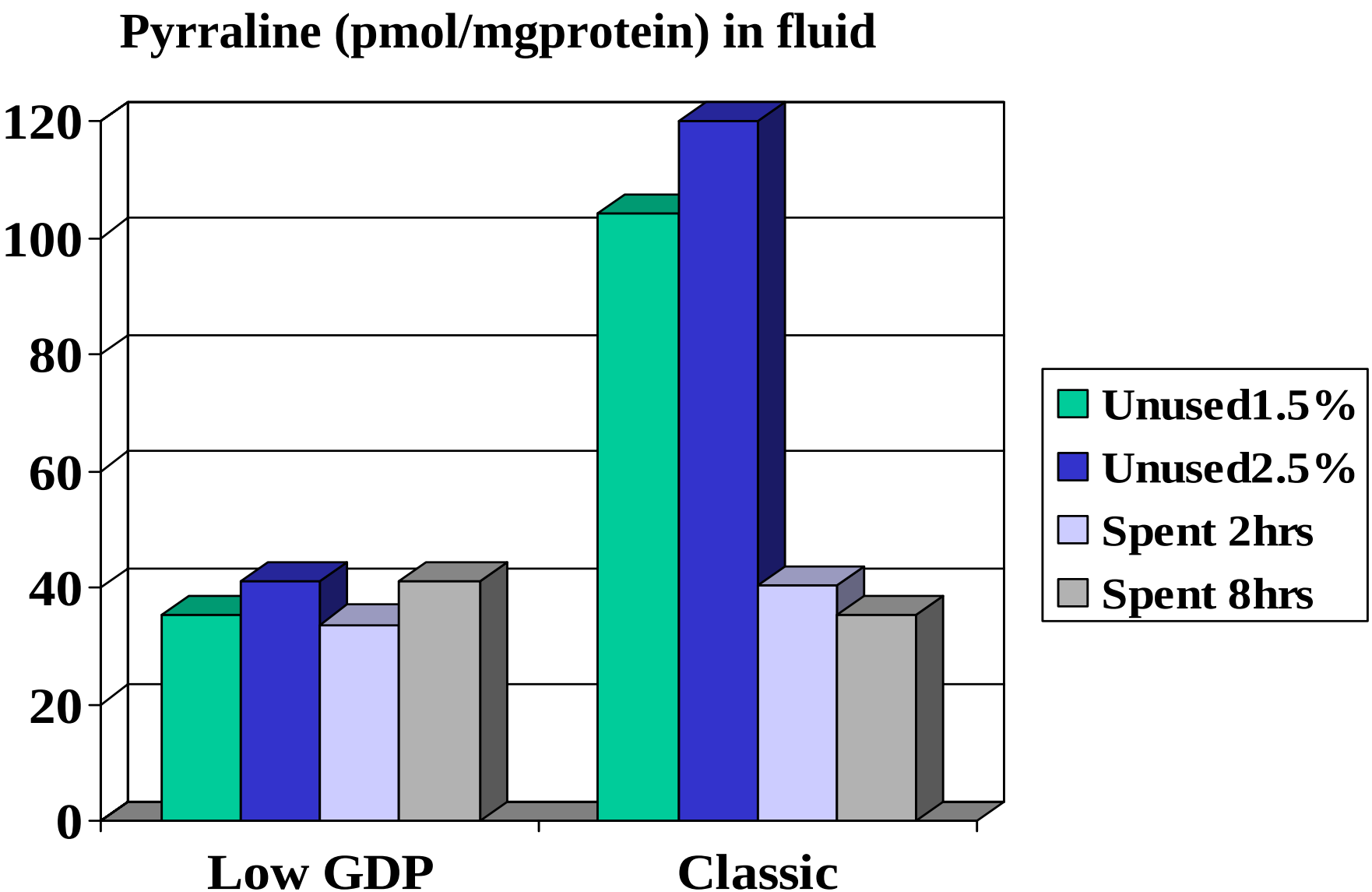
48

Davies et al, NDT, 11, 498-506, 1996.



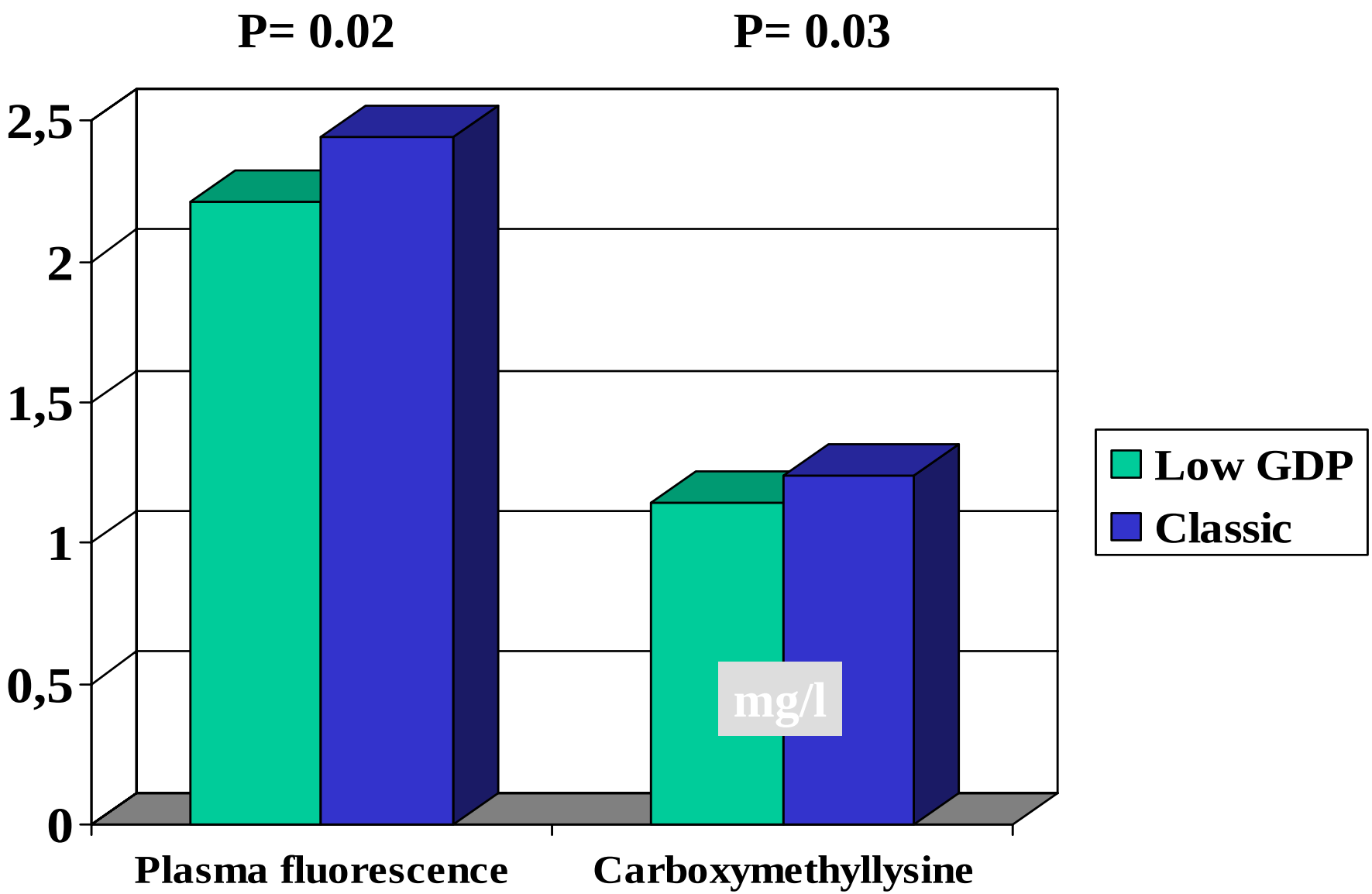
"Who was first?"

AGE's and GDP



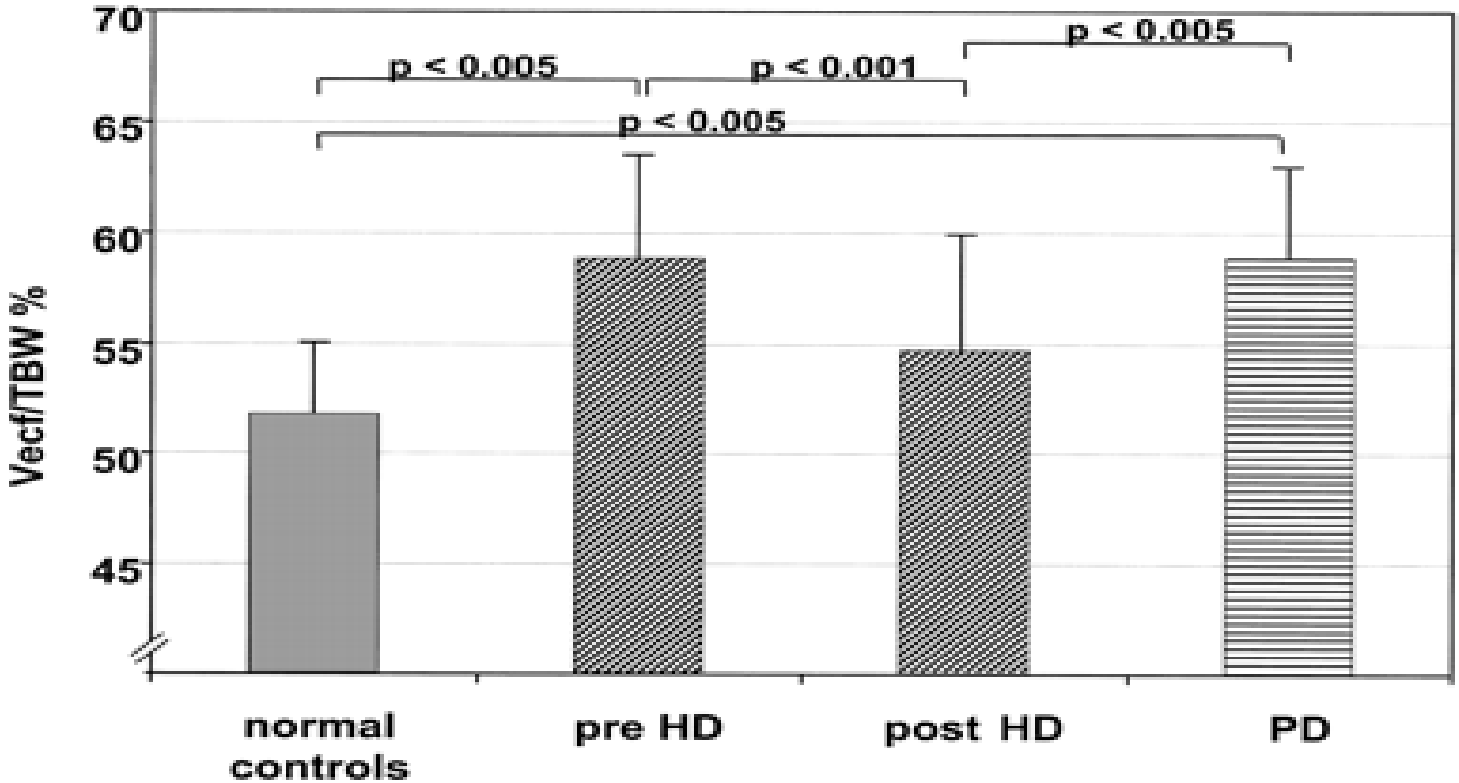
- Zeier et al, Kidney Int, 63, 298-305

AGE's and GDP



Zeier et al, Kidney Int, 63, 298-305

PD patients are (were?) often overhydrated

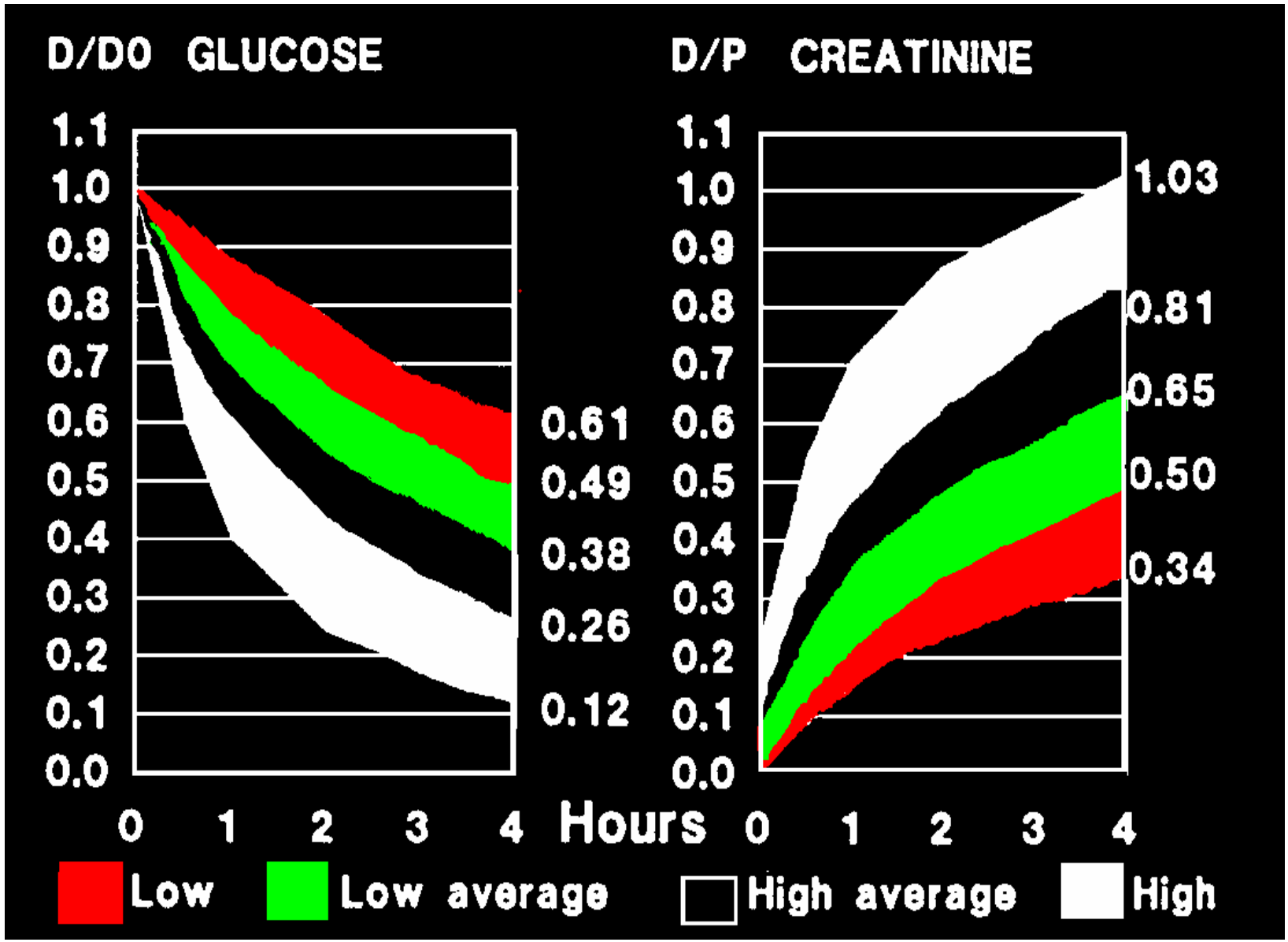


	normal controls	pre HD	post HD	PD
Recf [Ω]	669 ± 95	599 ± 90*$	693 ± 104#	548 ± 104$
Ricf [Ω]	1261 ± 278	1524 ± 388$	1453 ± 330	1372 ± 347
Rinf [Ω]	459 ± 70	426 ± 66	466 ± 58#	387 ± 66$

Level of significance p < 0.05 or better: $ HD or PD vs. Controls, * pre HD vs. post HD, # post HD vs. PD

Plum; NDT 2001

PET test.


D/D0 GLUCOSE
D/P CREATININE
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.61
0.49
0.38
0.26
0.12
1.03
0.81
0.65
0.50
0.34
0 1 2 3 4 Hours 0 1 2 3 4
Low
Low average
High average
High

INCREASING GLUCOSE CONCENTRATION IS ALWAYS BEST WHEN ULTRAFILTRATION IS INSUFFICIENT

Types of UF failure

- **Large vascular surface area**
- **A decreased osmotic conductance by glucose**
- **High disappearance rate of macromolecular structures (lymphatic absorption)**
- **Exremely small peritoneal surface area (e.g.adhesions)**

Krediet et al. PDI, 20, S22-S42, 2000

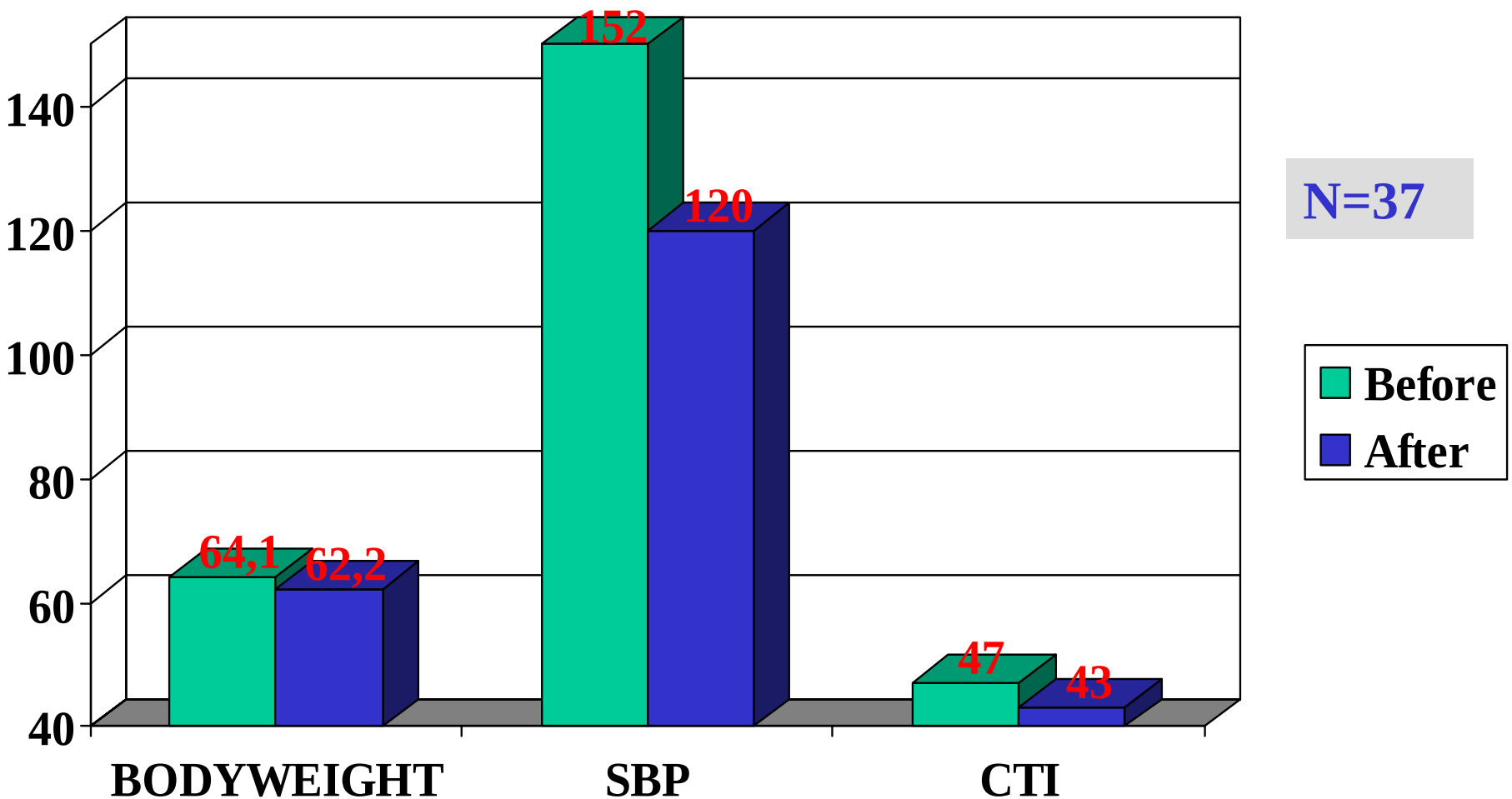
UF Failure

Clinical UF-Failure

Initial evaluation for reversible causes

- **Dietary incompliance salt/fluid**
  - Deficient education
  - Complex regimen
  - Burn-out
- Approriate **prescription**
  - **Dwell time**
  - **Dialysate tonicity**
- **Mechanical problems**
  - Leaks
    Entrapment
    Obstruction
    Malposition

Impact of dietary instructions on salt intake



Gunal et al, AJKD, 37, 2001, 588-593

Salt restriction and left ventricular hypertrophy

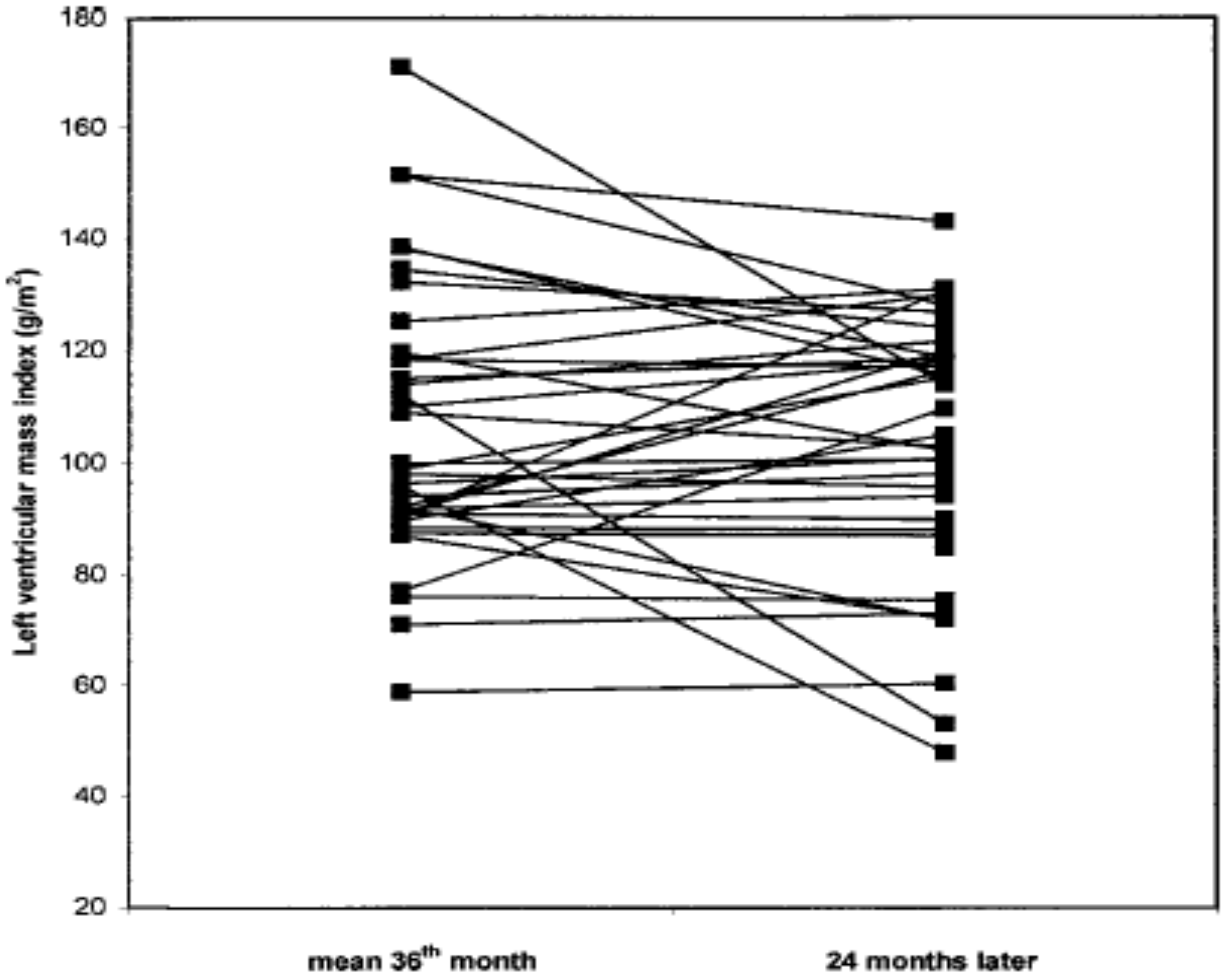


Figure 1 — Comparison of the echocardiographic (Echo) data of long-term peritoneal dialysis (PD) patients: baseline Echo was performed by mean 36th month of PD; the second Echo was performed 24 months later.

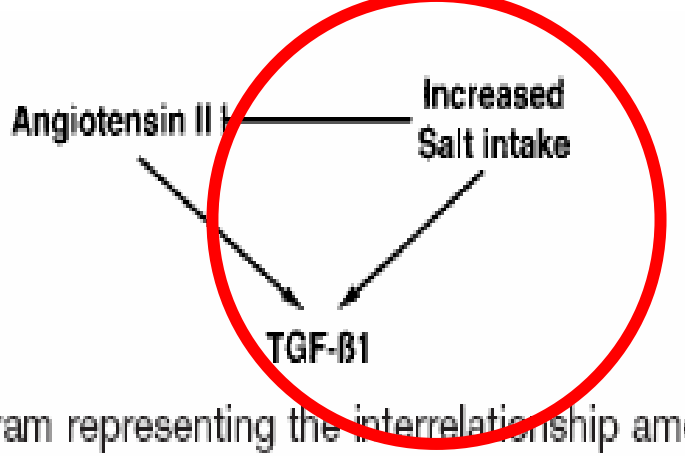


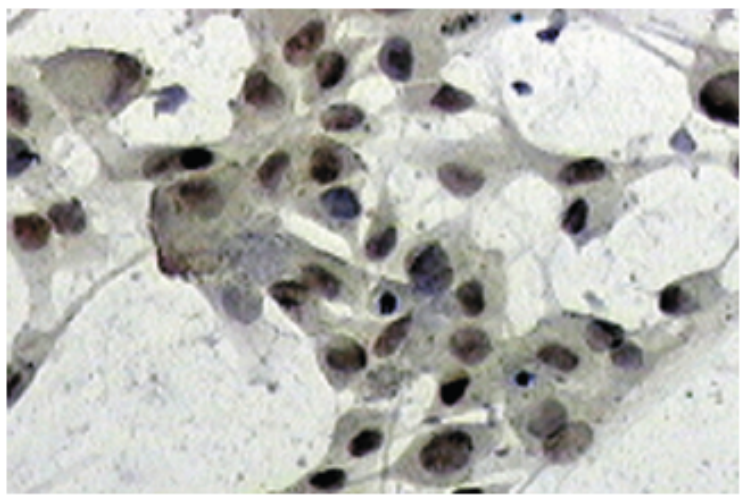
Figure 1. Diagram representing the interrelationship among dietary salt intake, the renin–angiotensin system, and renal TGF-β1 production. While the relationship between salt intake and angiotensin II is well appreciated, perhaps the ability of angiotensin II and increased salt intake to stimulate independently production of TGF-β1 is less well appreciated. In an attempt to control intrarenal production of TGF-β1, both pathways should be considered.

Sanders et al, Hypertension, 2006

Ksiazek et al, Lab Invest, 2007

TGF-β regulates glucose-induced senescence of mesothelial cells in dialysis patients

See page 345



Insulin need in diabetic patients after start of PD: Relation to hypertonic bag use

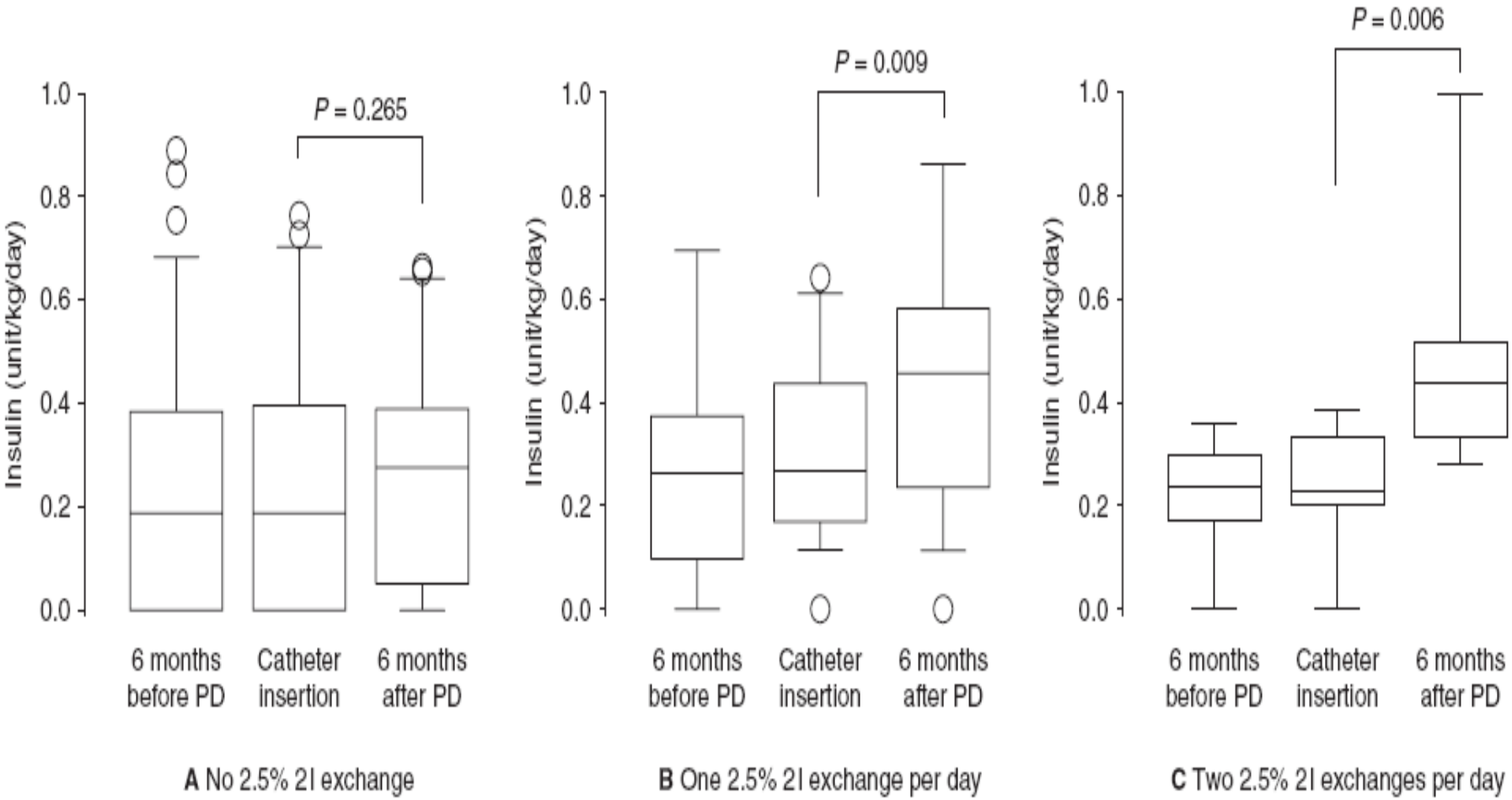
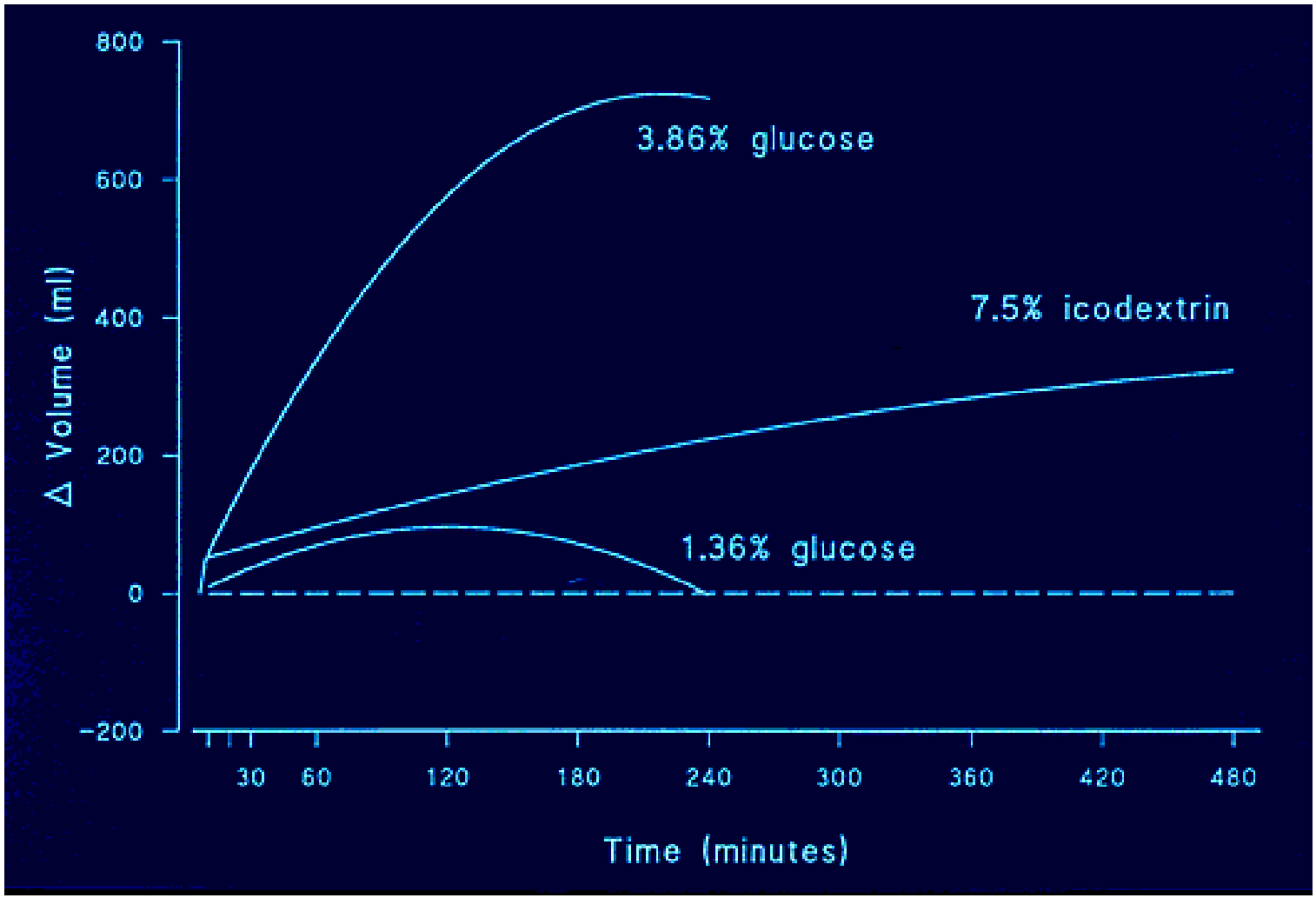
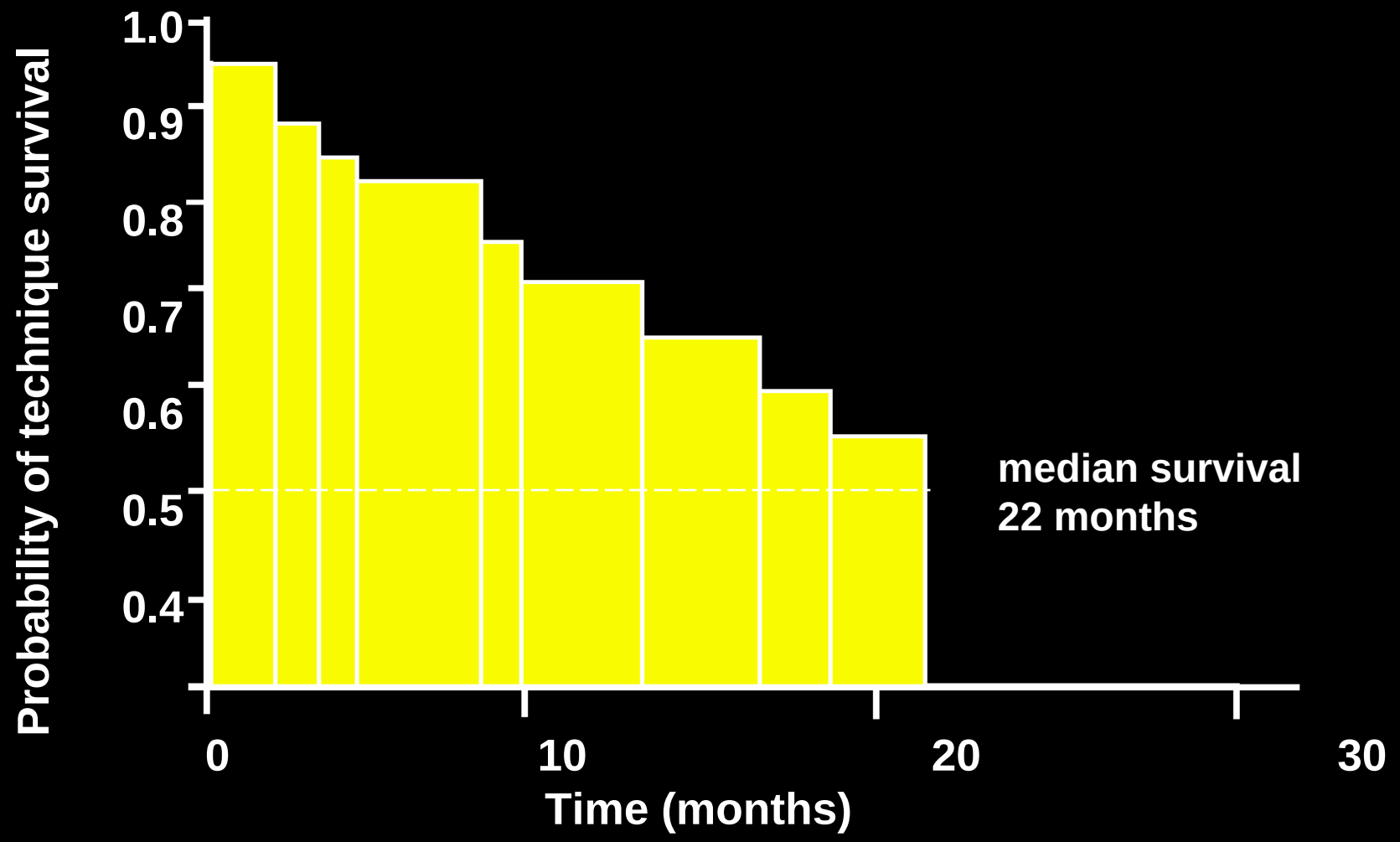


Fig. 3. The relation between change in insulin requirement and number of 2.5% 2l exchanges per day. All patients received a standard 2l exchange three times daily.

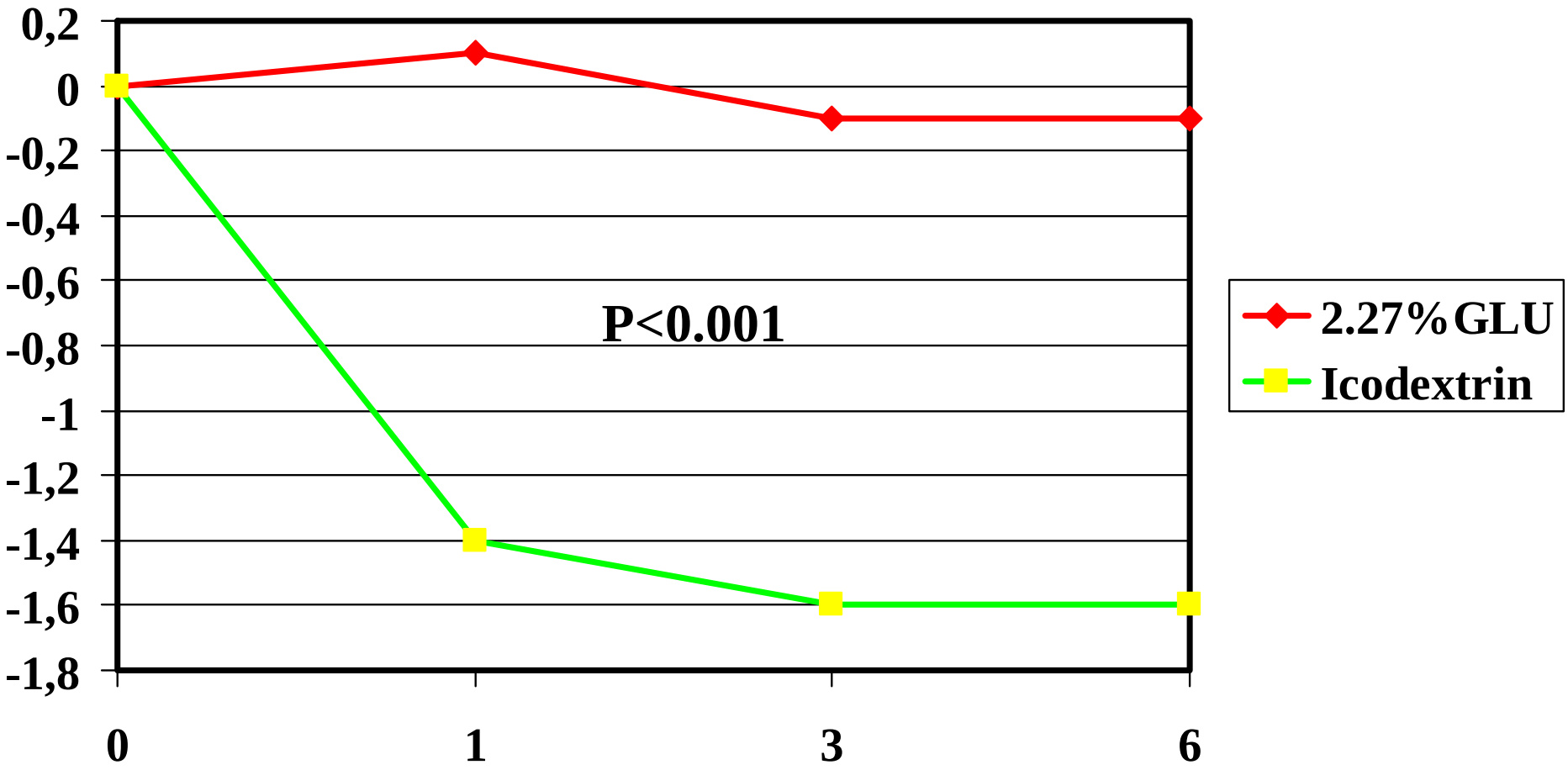

800
600
400
200
0
-200
Δ Volume (ml)
3.86% glucose
7.5% icodextrin
1.36% glucose
30
60
120
180
240
300
360
420
480
Time (minutes)

Extensions of PD technique survival in 53 patients with UF failure using Icodextrin (Extraneal).



Wilkie et al, PDI, 17, 1, 86, 1997.

Evolution of TBW after start of Extraneal



Davies et al. JASN, 14, 2338-2344, 2003

S. B. is a 28 year old woman who has had renal failure since adolescence, and high panel reactivity since a failed transplant 15 years ago. After 10 years on haemodialysis she developed major problems with vascular access and switched to PD in March 1992. Latterly she has had increasing problems with fluid balance.

PET: Date	4 hour D/P creatinine ratio	UF Capacity ml
1993	0.62	400
1994	0.5	430
1995	0.55	250
1996	0.72	220
1997	0.85	-100
1998	0.79	100

Plot the progressive change in peritoneal kinetics, and identify cause of ultrafiltration failure. Design a regime that will improve fluid balance problems.

Ultrafiltration failure

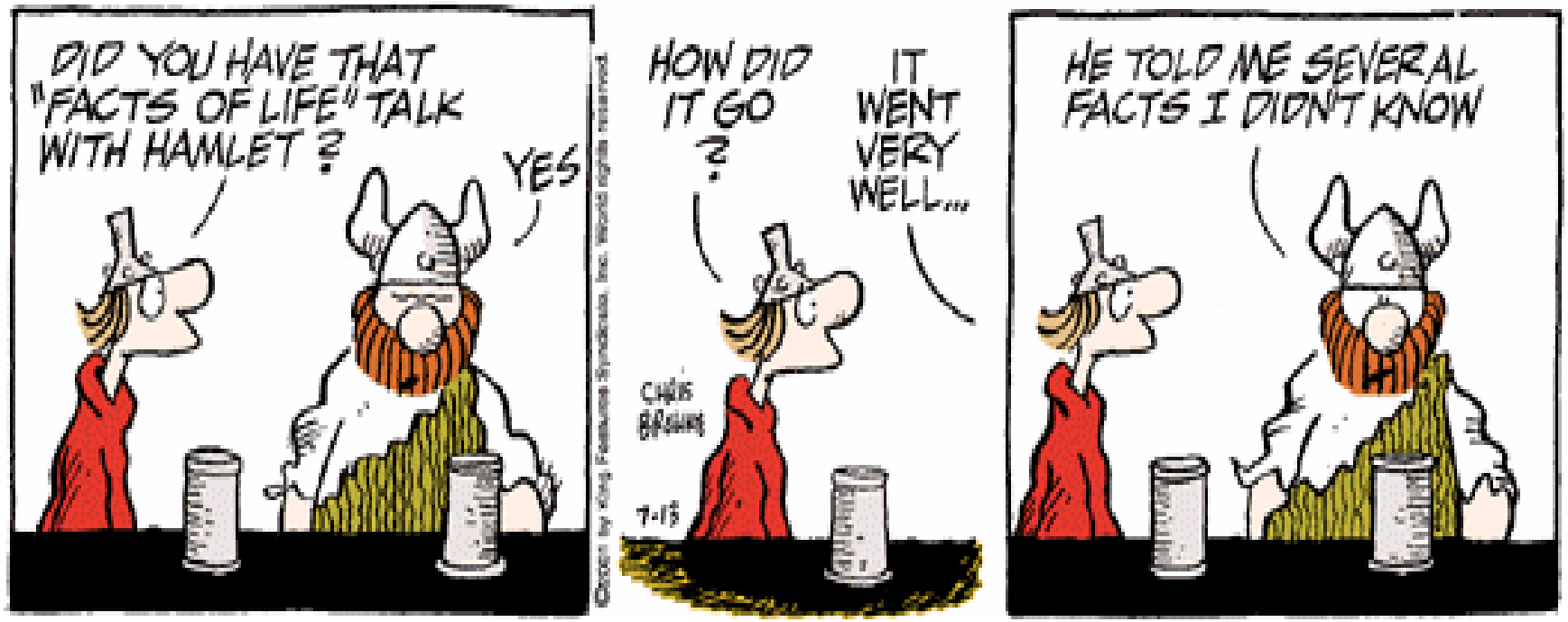
Mr Jones, weight gain 1.5kg over two days

Dialysate	Normal UF	UF obtained yesterday
1.36%	-100	-300
1.36%	0	-350
1.36%	-100	-325
Extraneal	400	-275

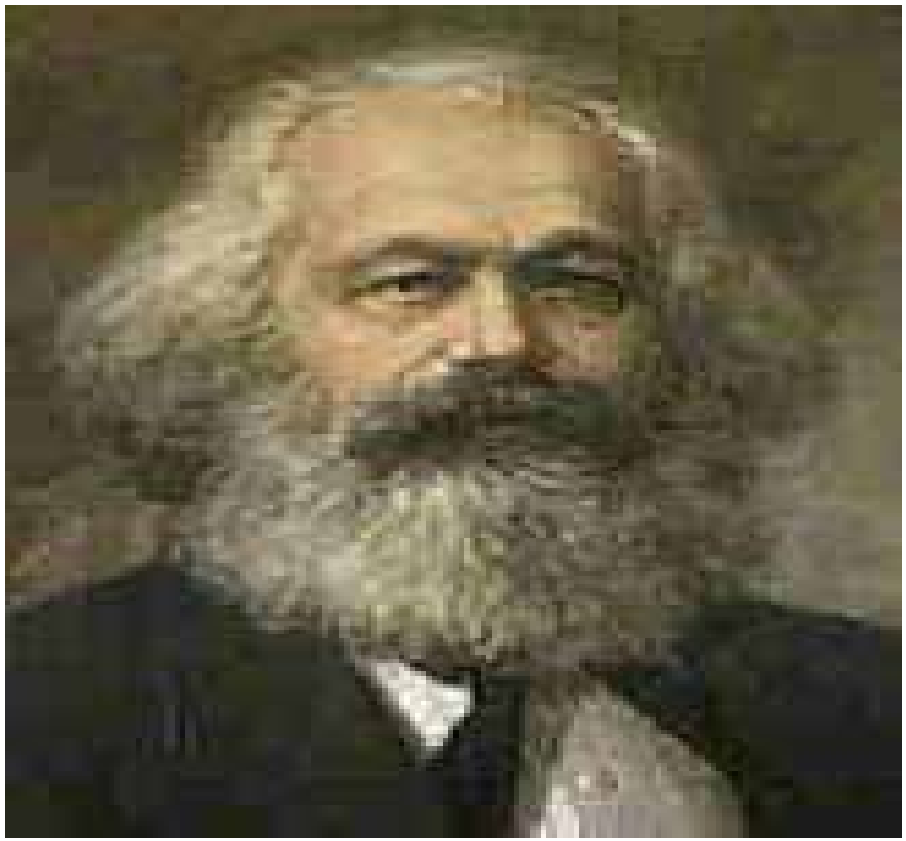
Ultrafiltration failure

Mr Jones, weight gain 1.5kg over two days

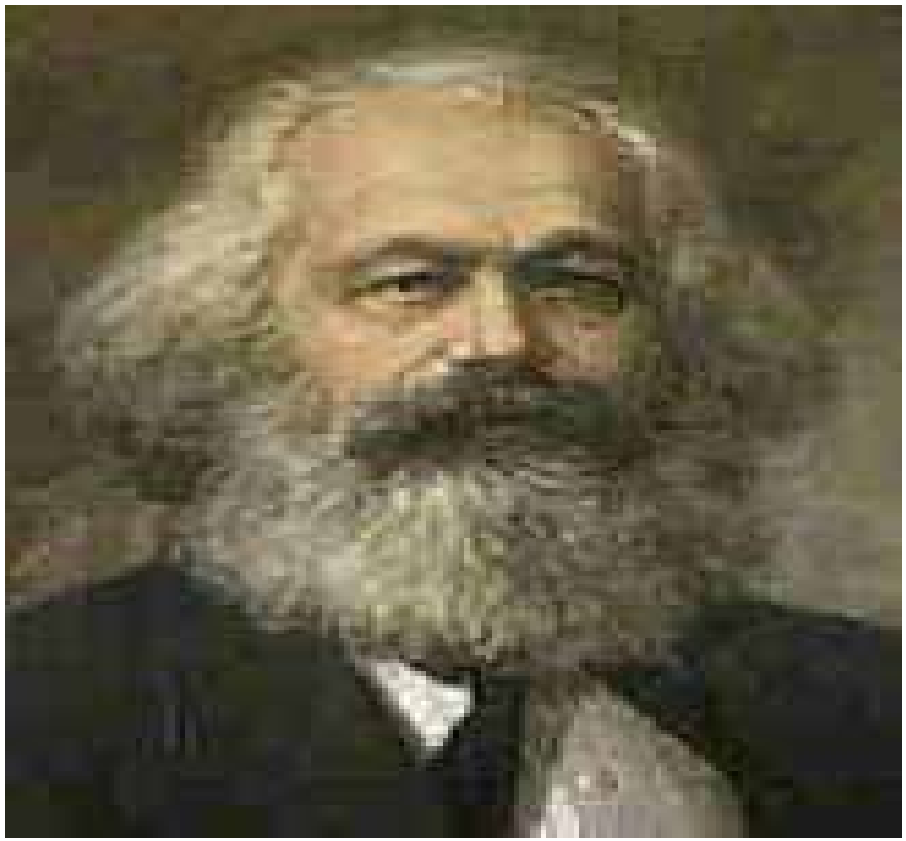
Dialysate	Normal UF	UF obtained yesterday
1.36%	-100	-300
1.36%	0	-350
1.36%	-100	-325
Extraneal	400	+750



Lessons to be learned

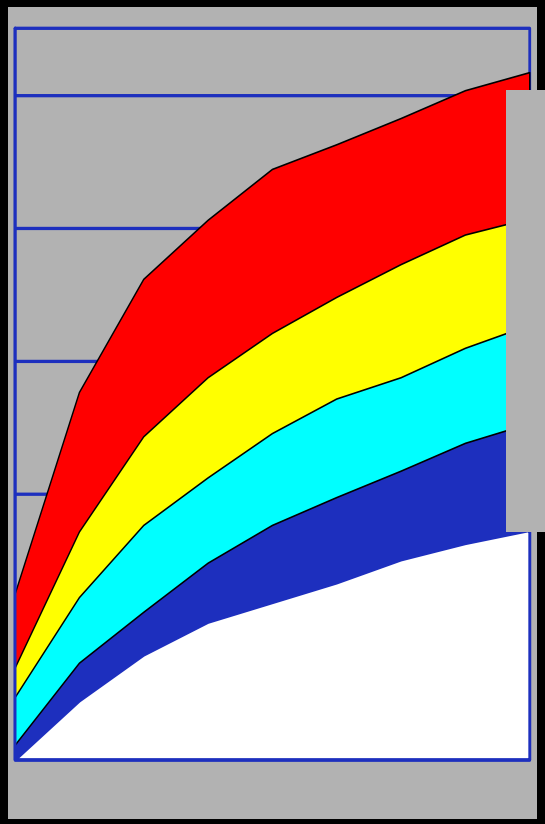


All patients should be equal



…but some should be more equal than others

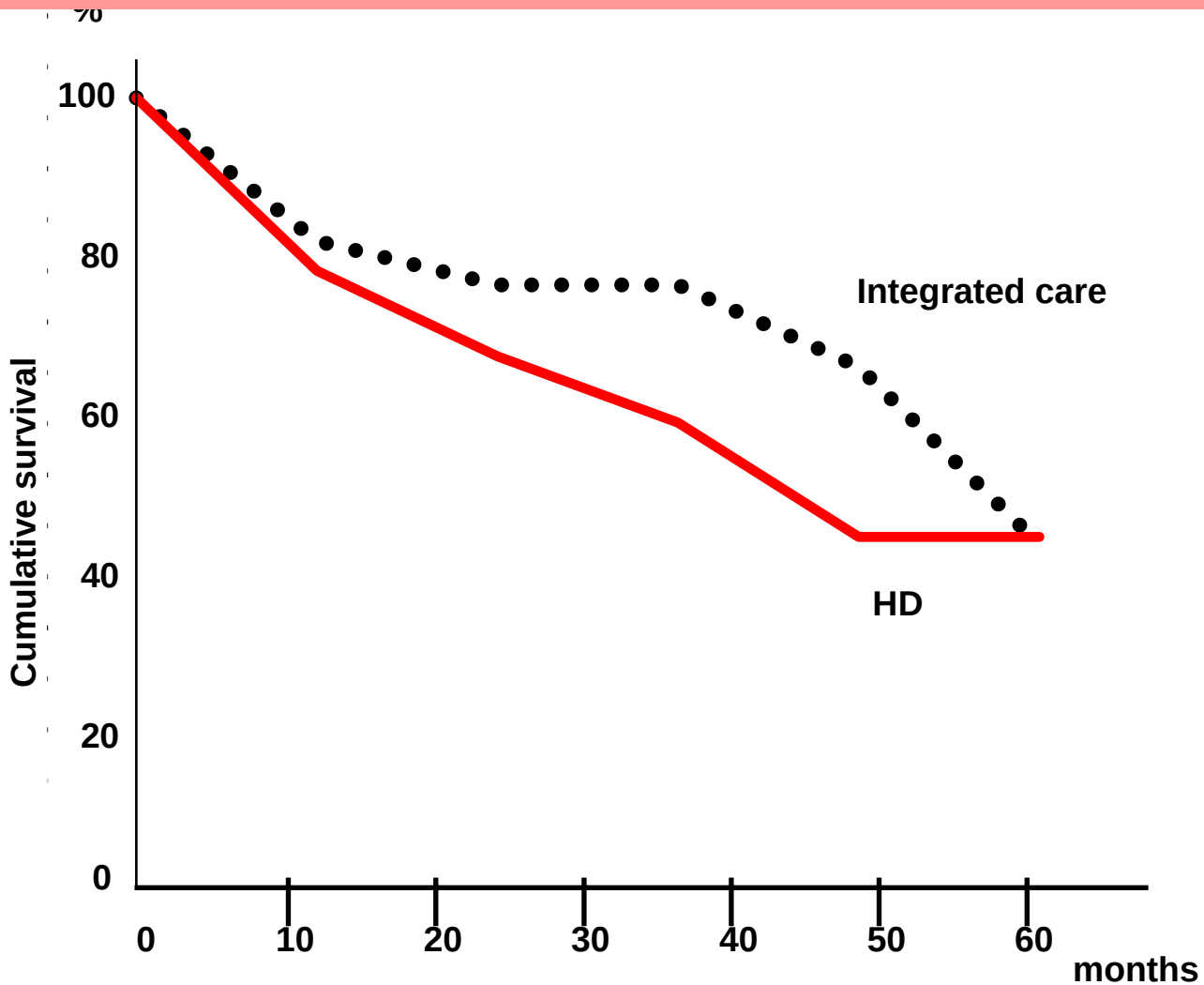
Recommendations



	CAPD	CCPD	NIPD	PD-Plus
High	−	−	+	+
High-a	+	+	±	+
Low-a	+	±	−	+
Low	±	−	−	±

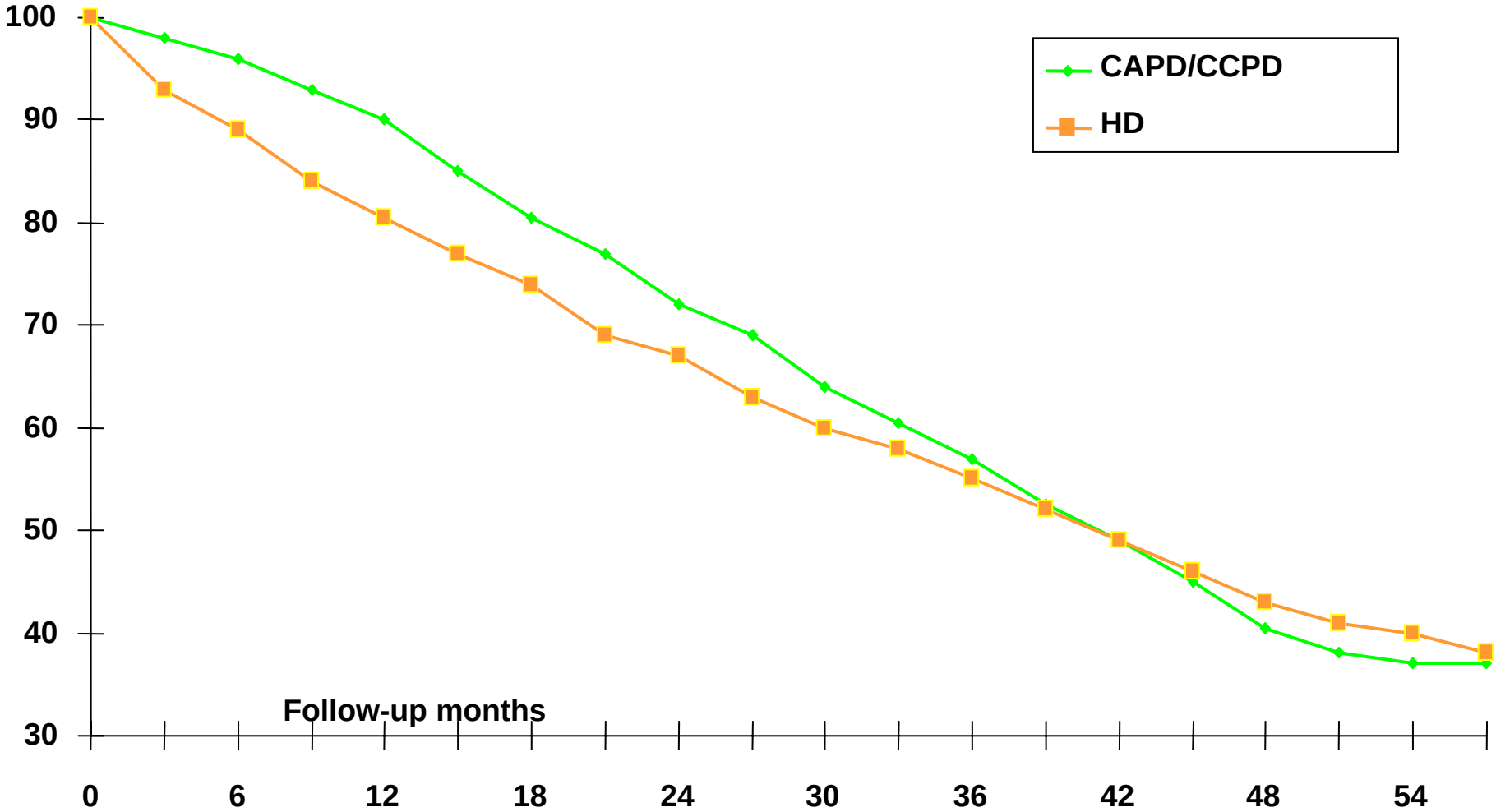
THE RIGHT TREATMENT FOR THE RIGHT PATIENT

Matched – Control Analysis
PD first vs HD



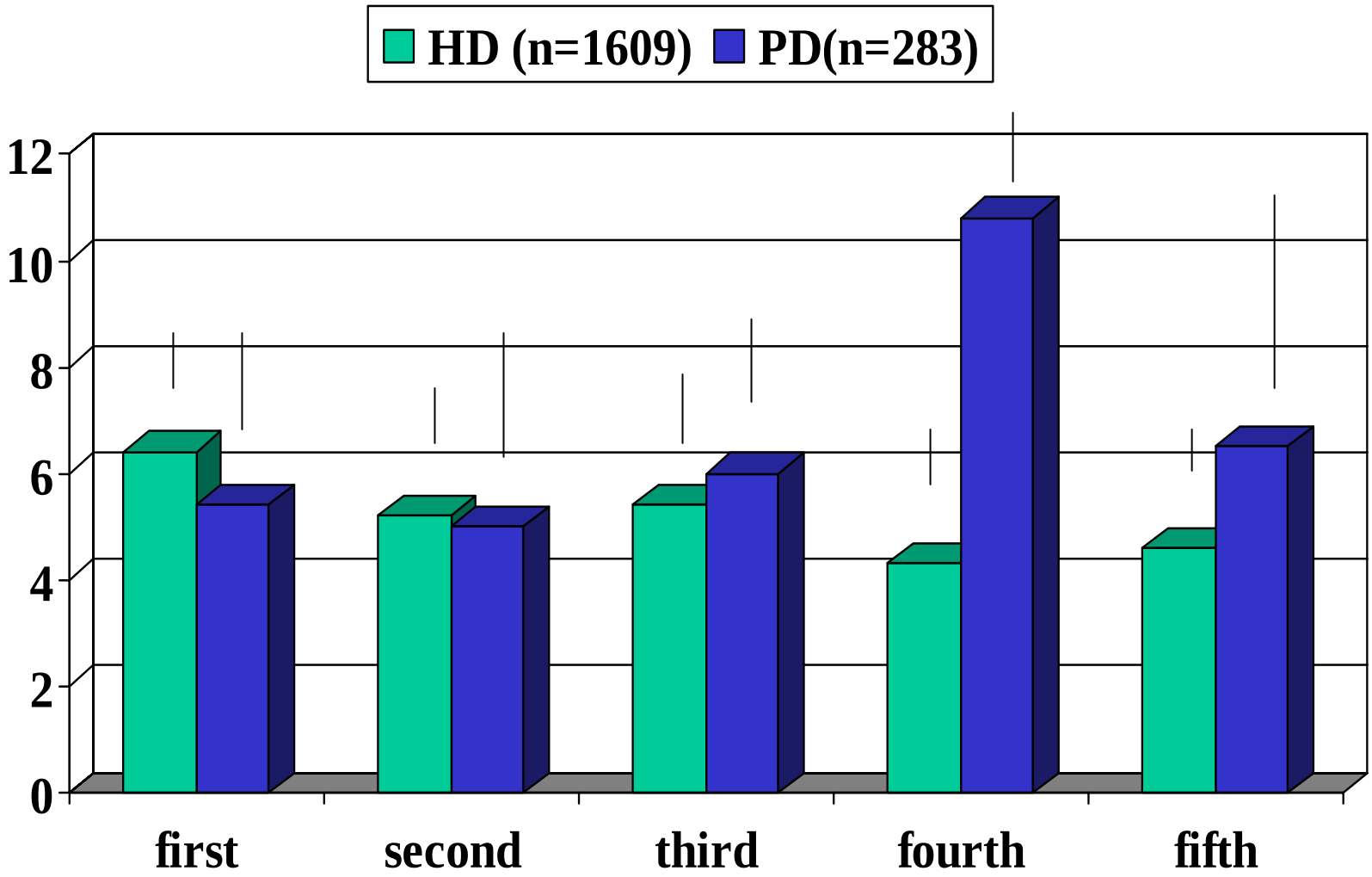
Van Biesen et al, JASN, 11, 116-125, 2000

Patient Survival Probability for Patients Initiating Dialysis with CAPD/CCPD Compared to Hemodialysis (1990-94)



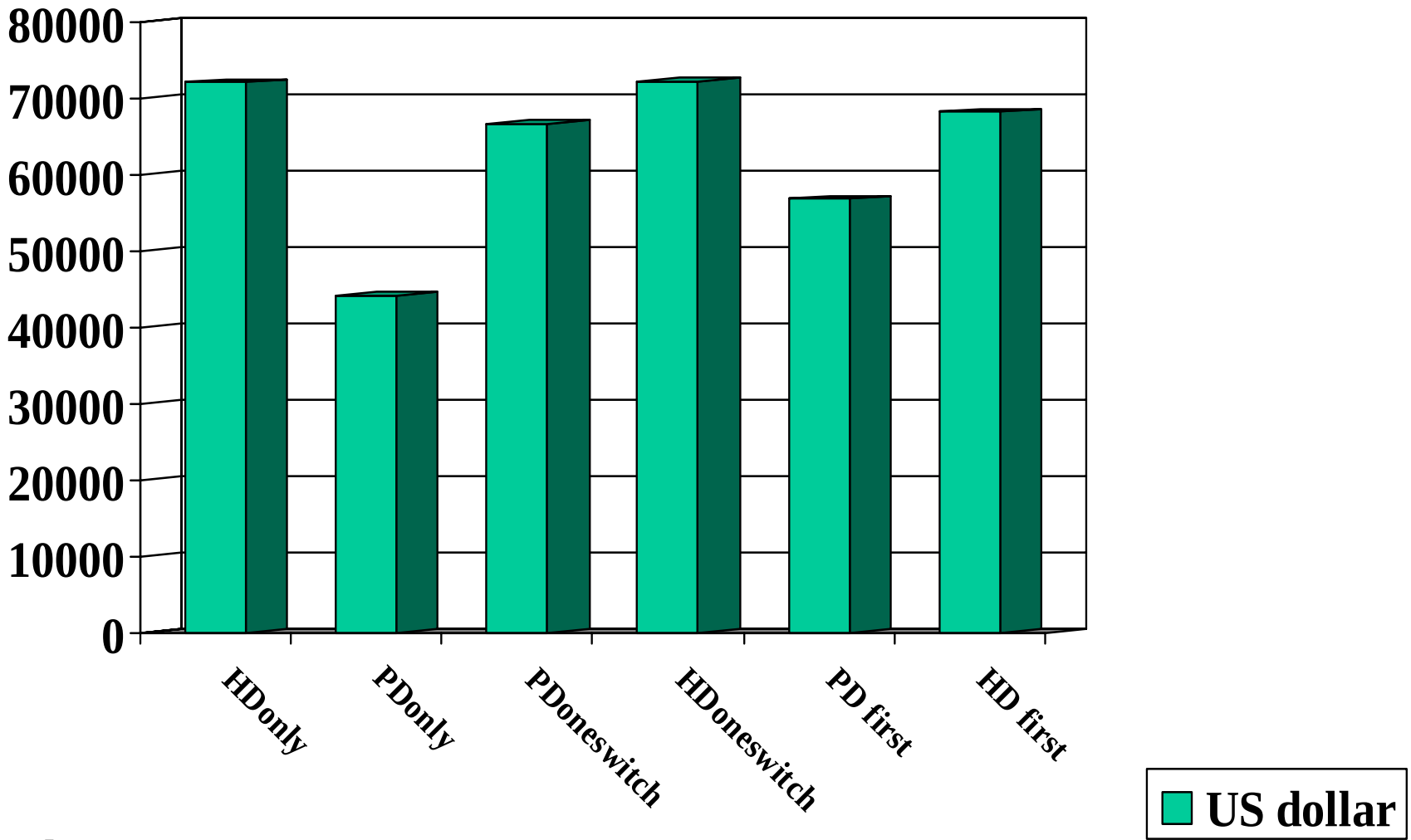
Fenton SA, et al, *Am J Kidney Dis*, 1997; 30:334-342

Standardized mortality ratio's of dialysis vs general population



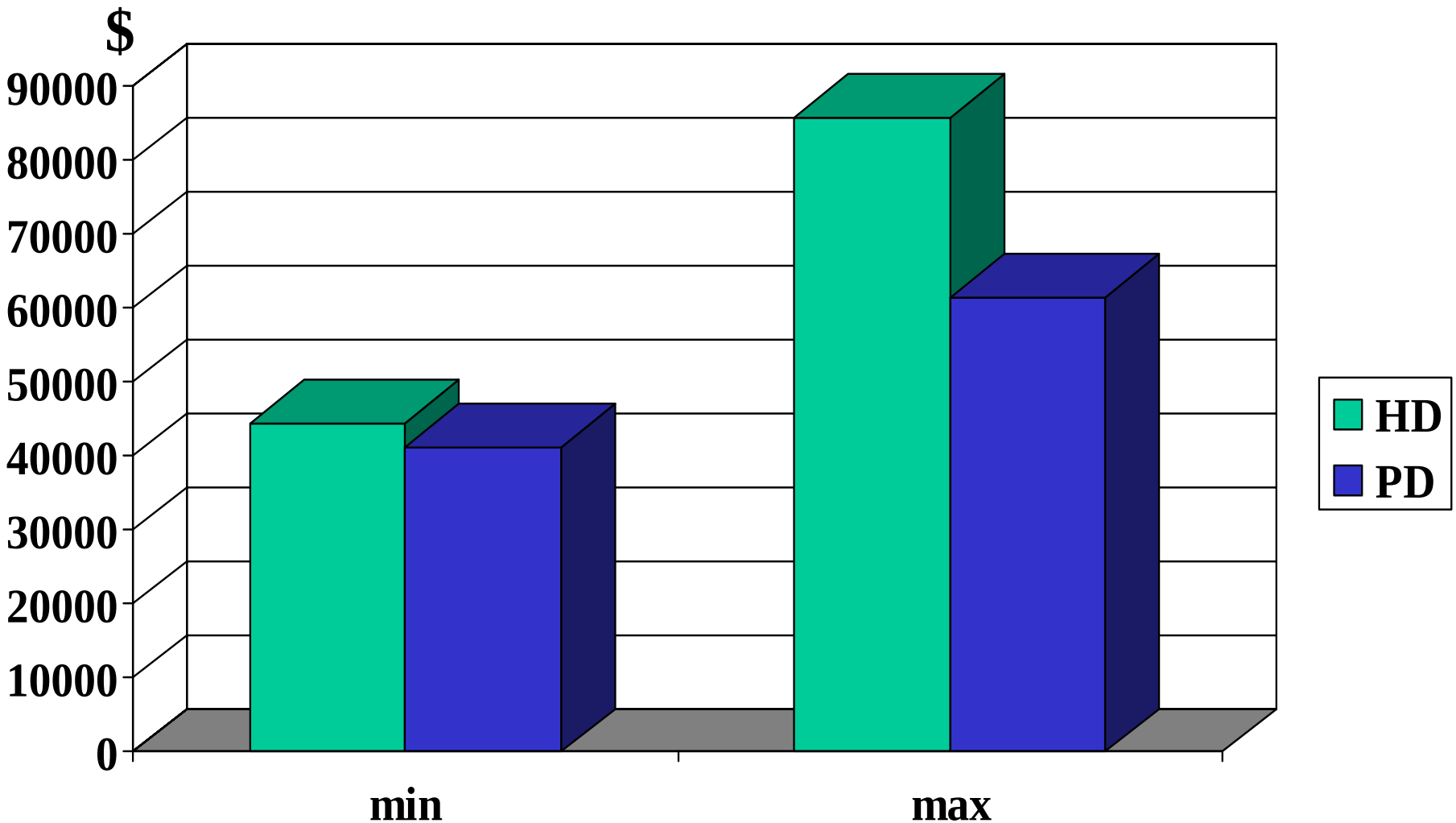
Villar et al, JASN 2007

Medicare expenditures and type of RRT



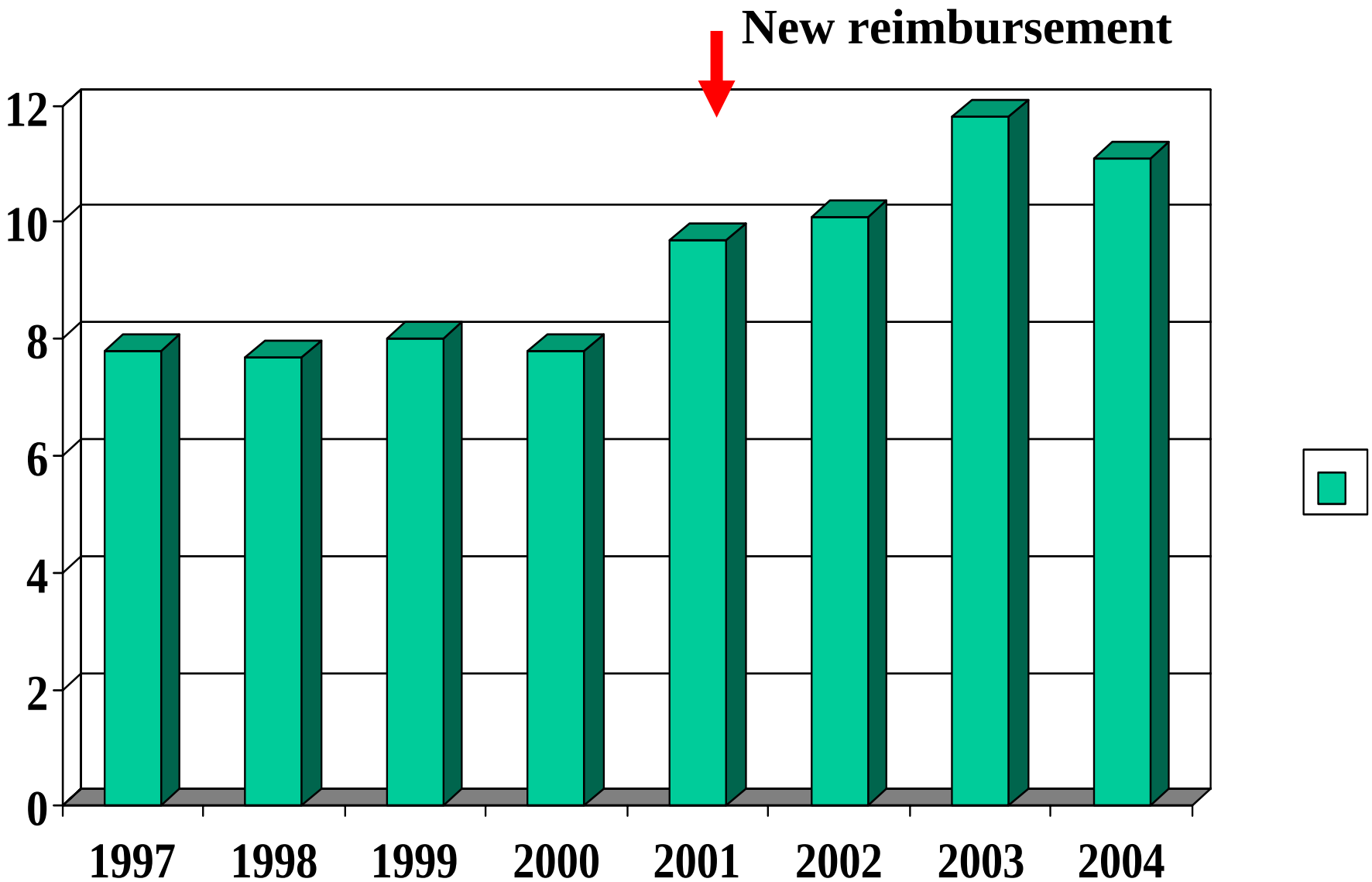
Shih et al, KI, 2005, 319

Cost/life year gained of PD vs HD in Finland: a matched pair analysis



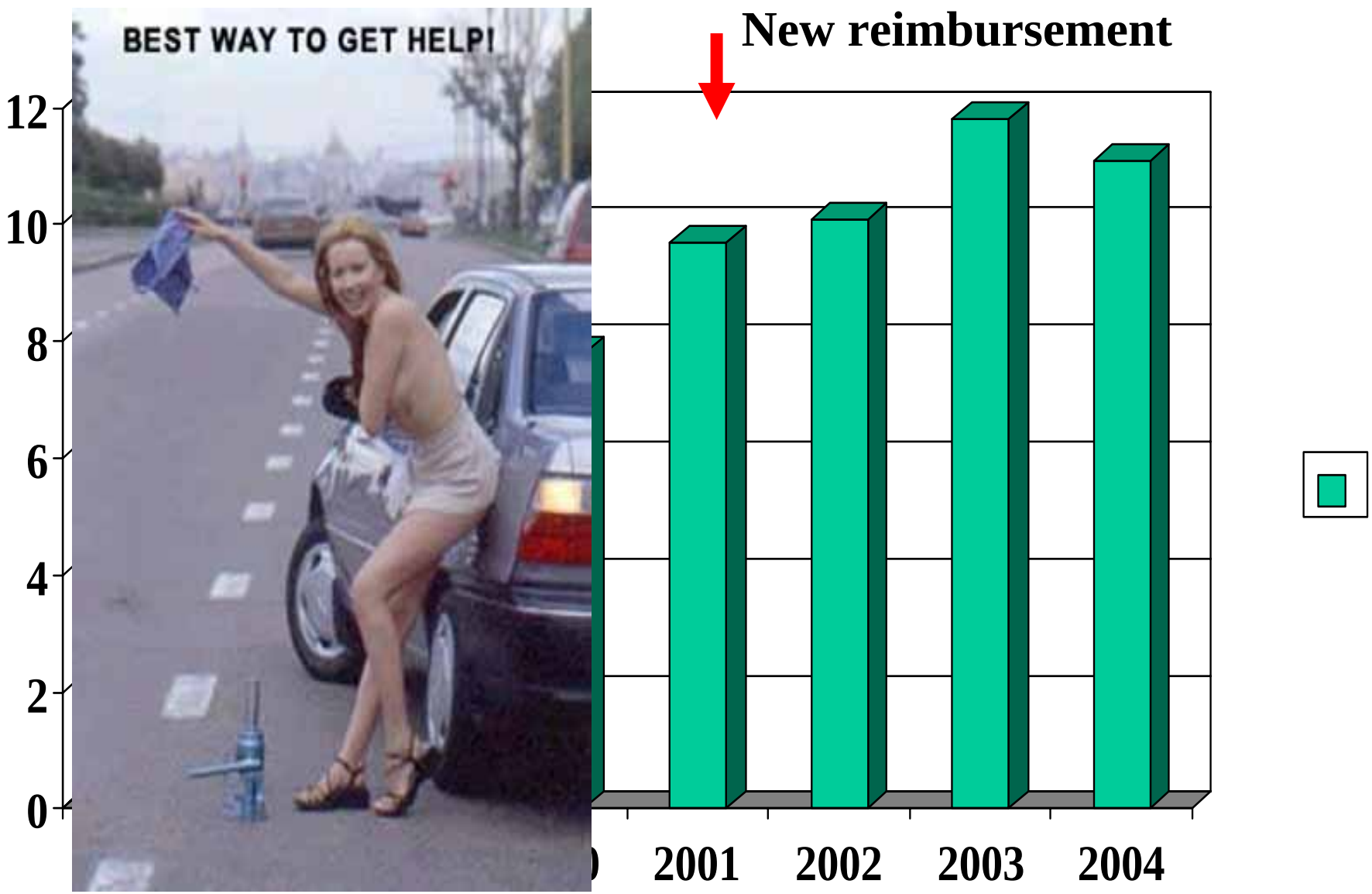
Salonen et al, Int J Urol Nephrol, 2007

PD distribution in Flanders



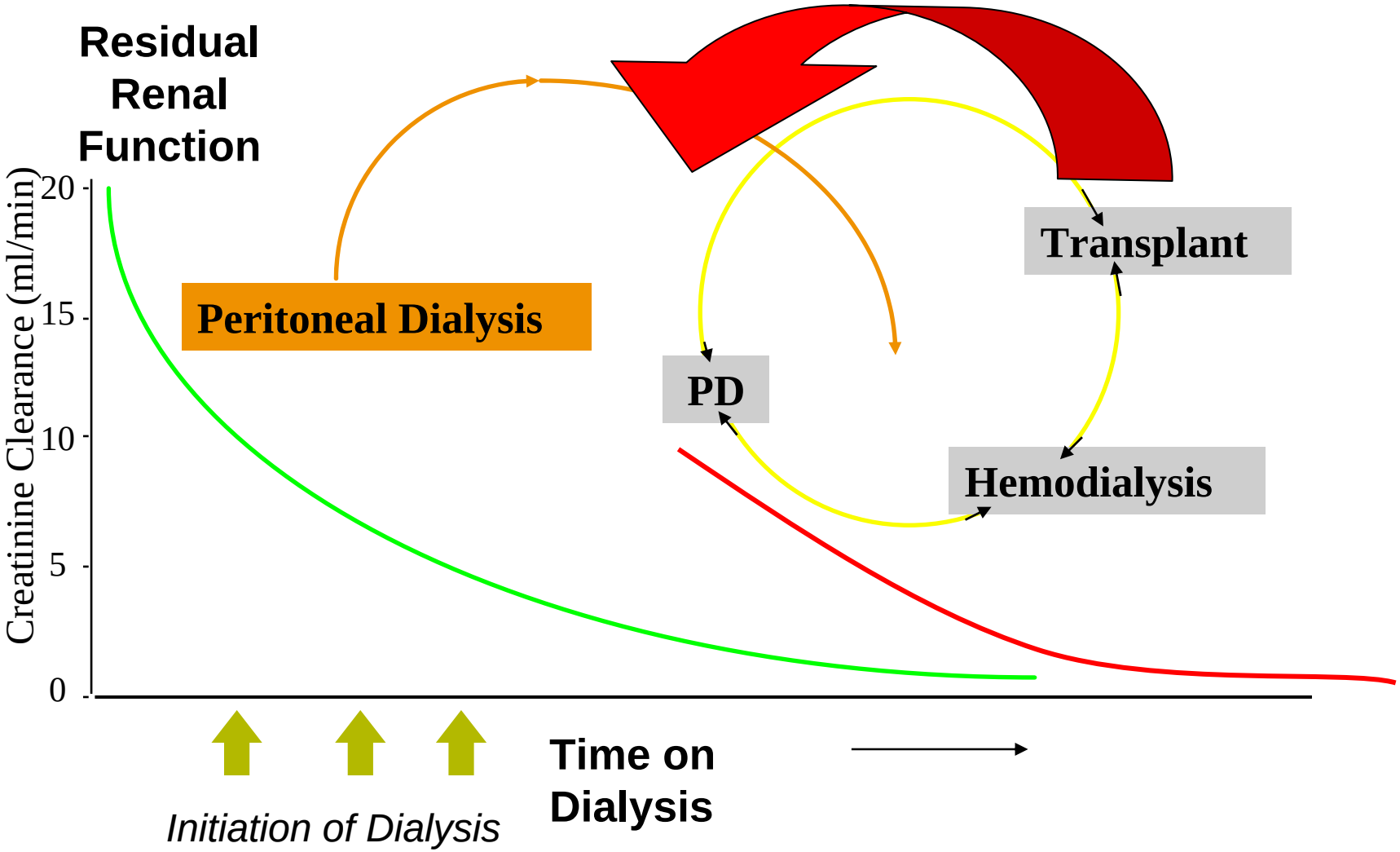
NBVN Registry

PD distribution in Flanders



NBVN Registry

The Context - within the Integrated Care Model



Potential advantages of PD for early start dialysis

- Cost benefit
- Negative effect of HD on residual renal function
- Preservation of vascular access
- Outcome after transplantation
- Lower risk for infection
- Incremental dialysis doses at lower costs
- Lifestyle benefits

Van Biesen et al, PDI

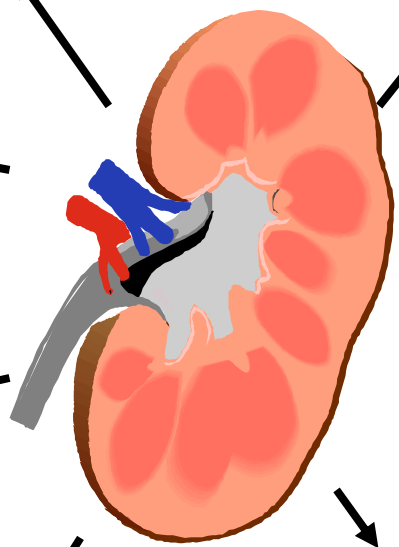
Benefits of Residual Renal Function

Provides endocrine functions

- *Erythropoietin production*
- *Ca^{++}, phosphorus and vitamin D homeostasis*

Contributes to total solute clearance *(1 ml/min CrCl = 10 liter CrCl/week)*

Reduces Mortality



Improves β_2-microglobulin and middle molecule clearance

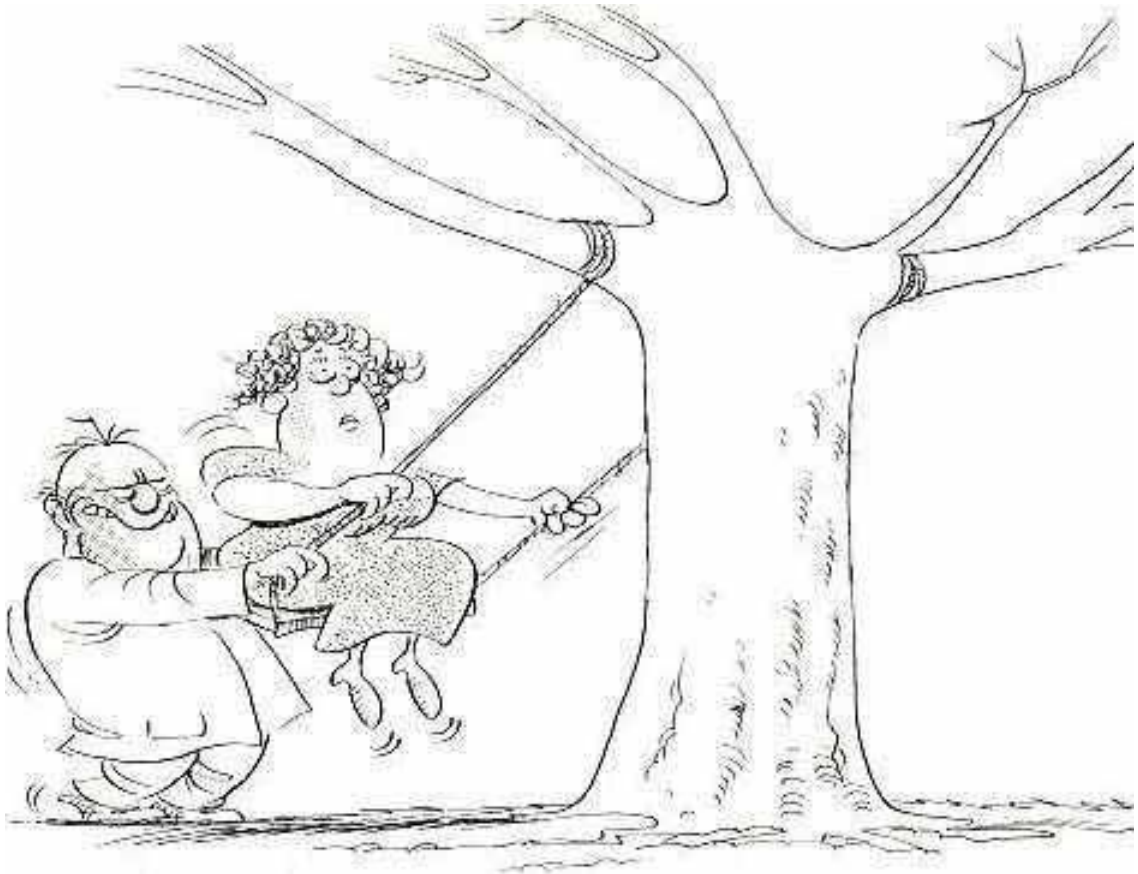
Improves QOL

Facilitates volume control

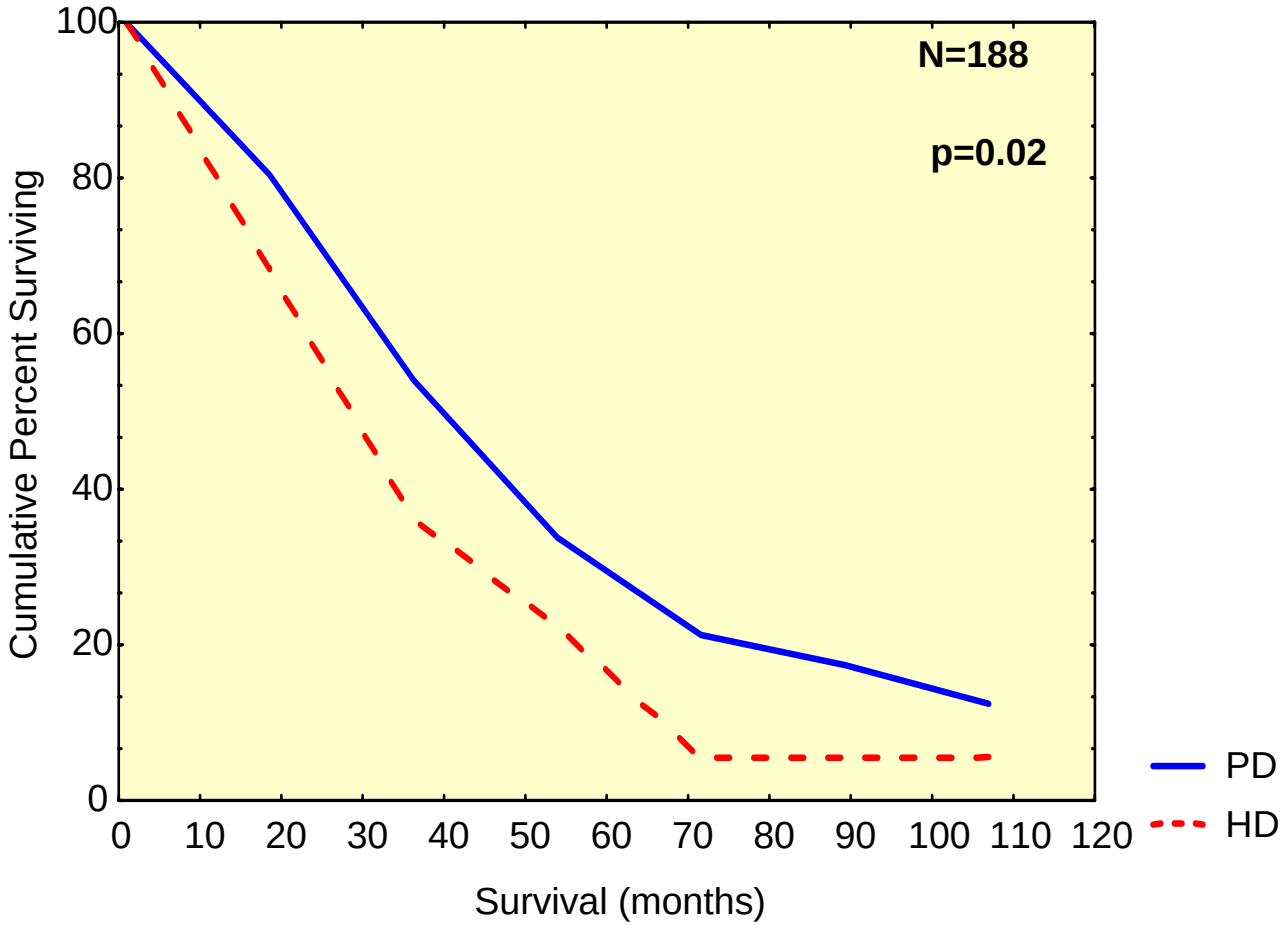
Increases nutritional status

Allows for more liberal diet and fluid intake

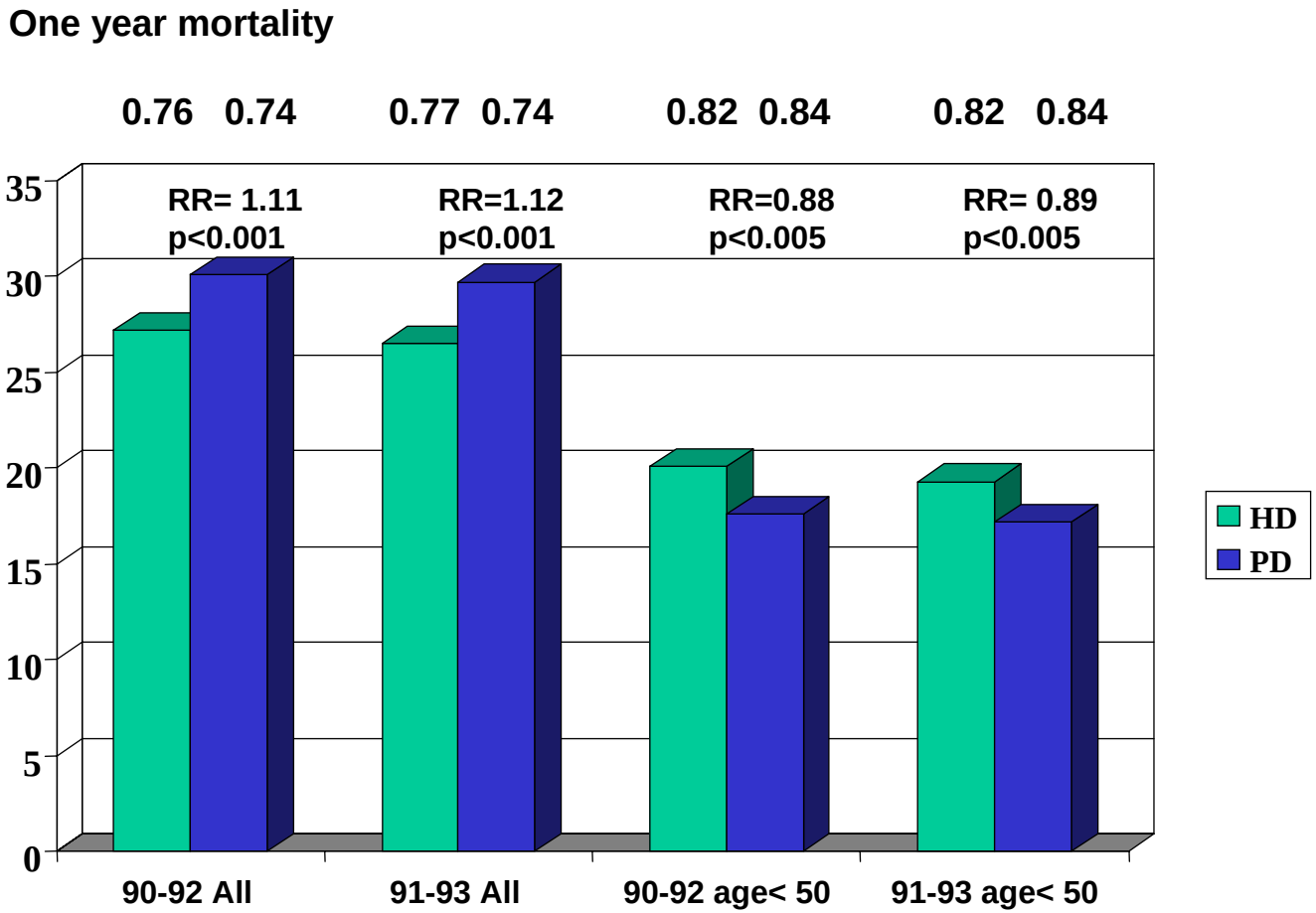
“ Free choice ”



Survival Diabetic patients Stoke/Gent/ Brescia

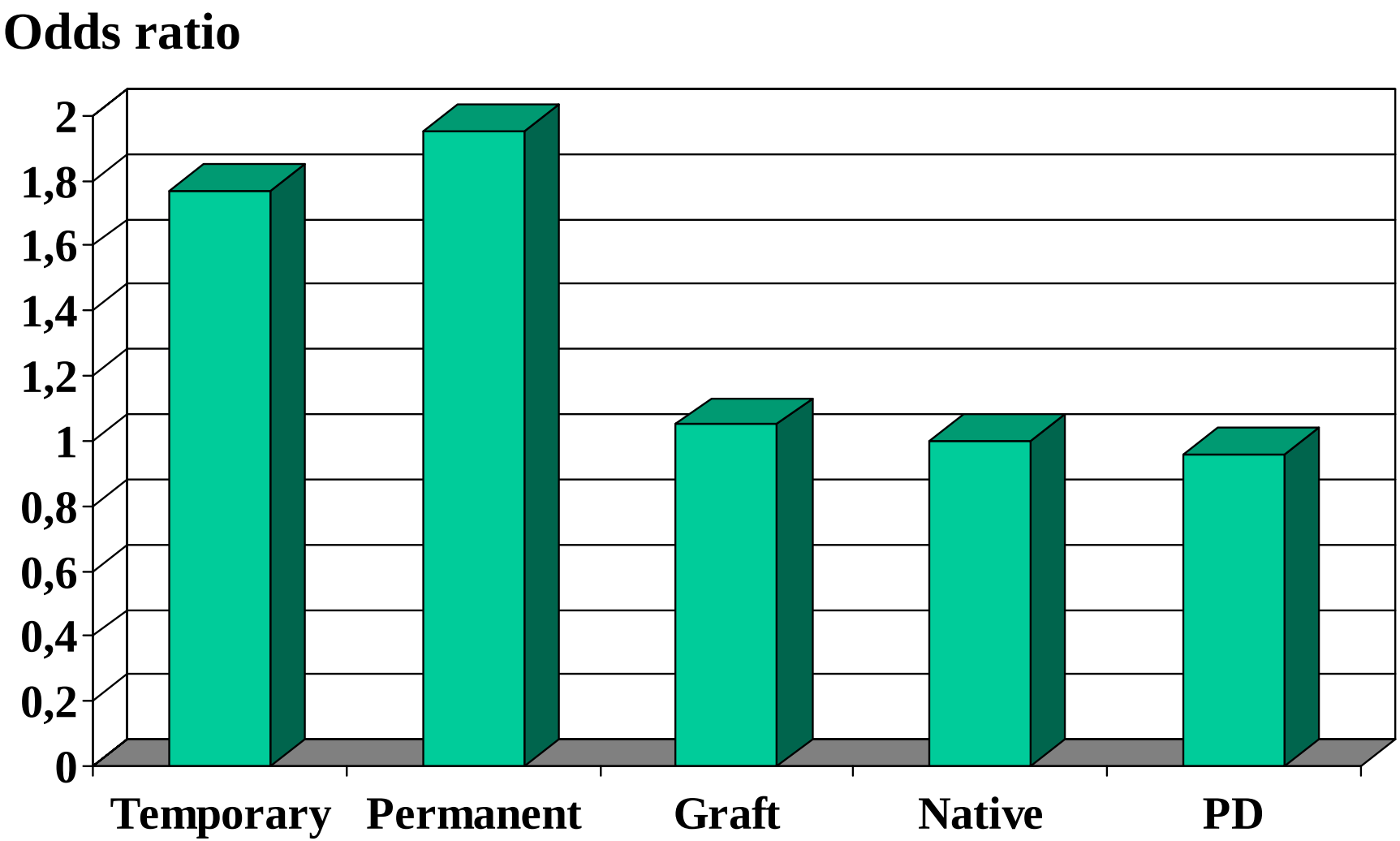


Diabetics



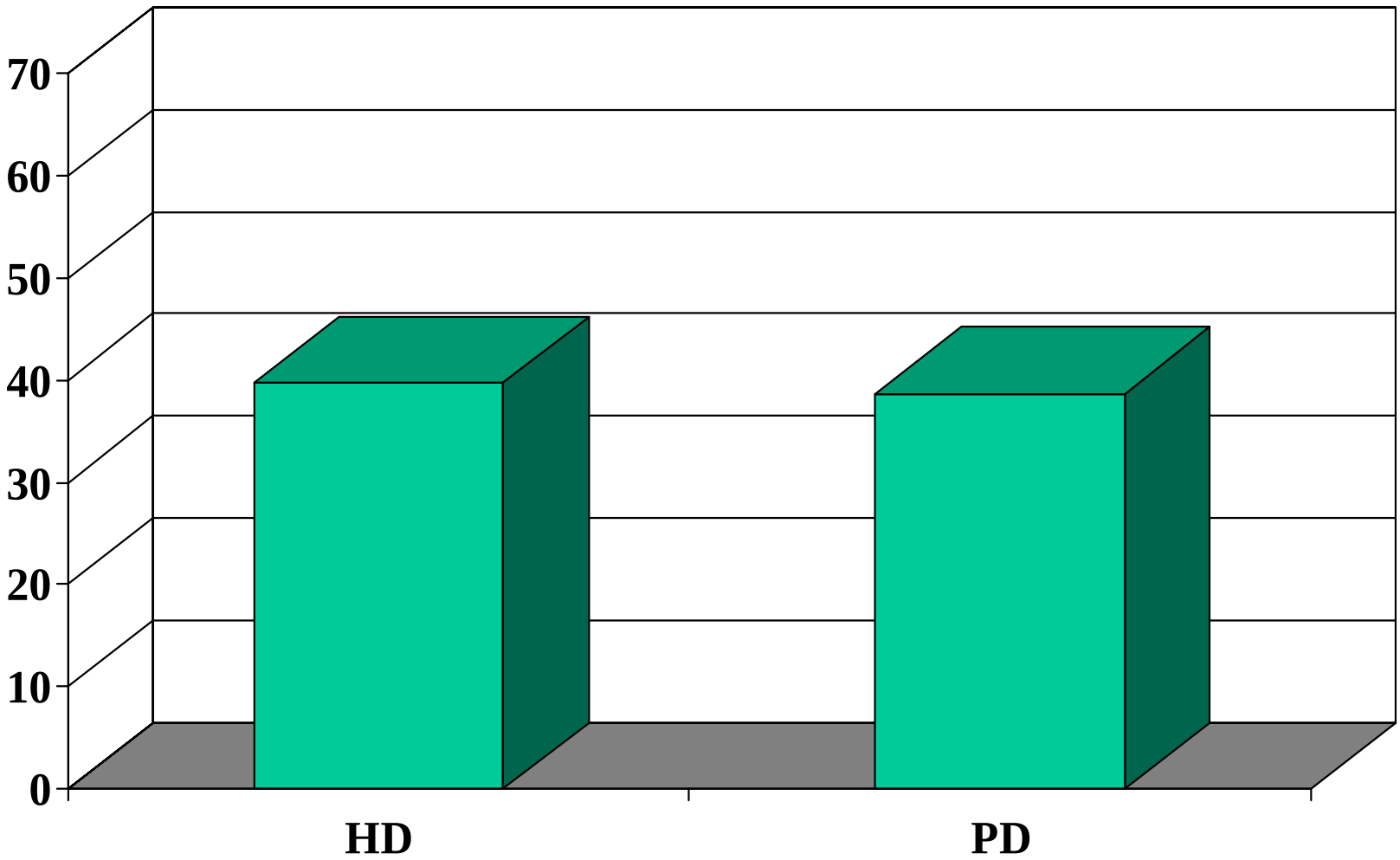
Vonesh et al, JASN, 10, 354-365, 1999

Access and septicemia in USRDS wave 2



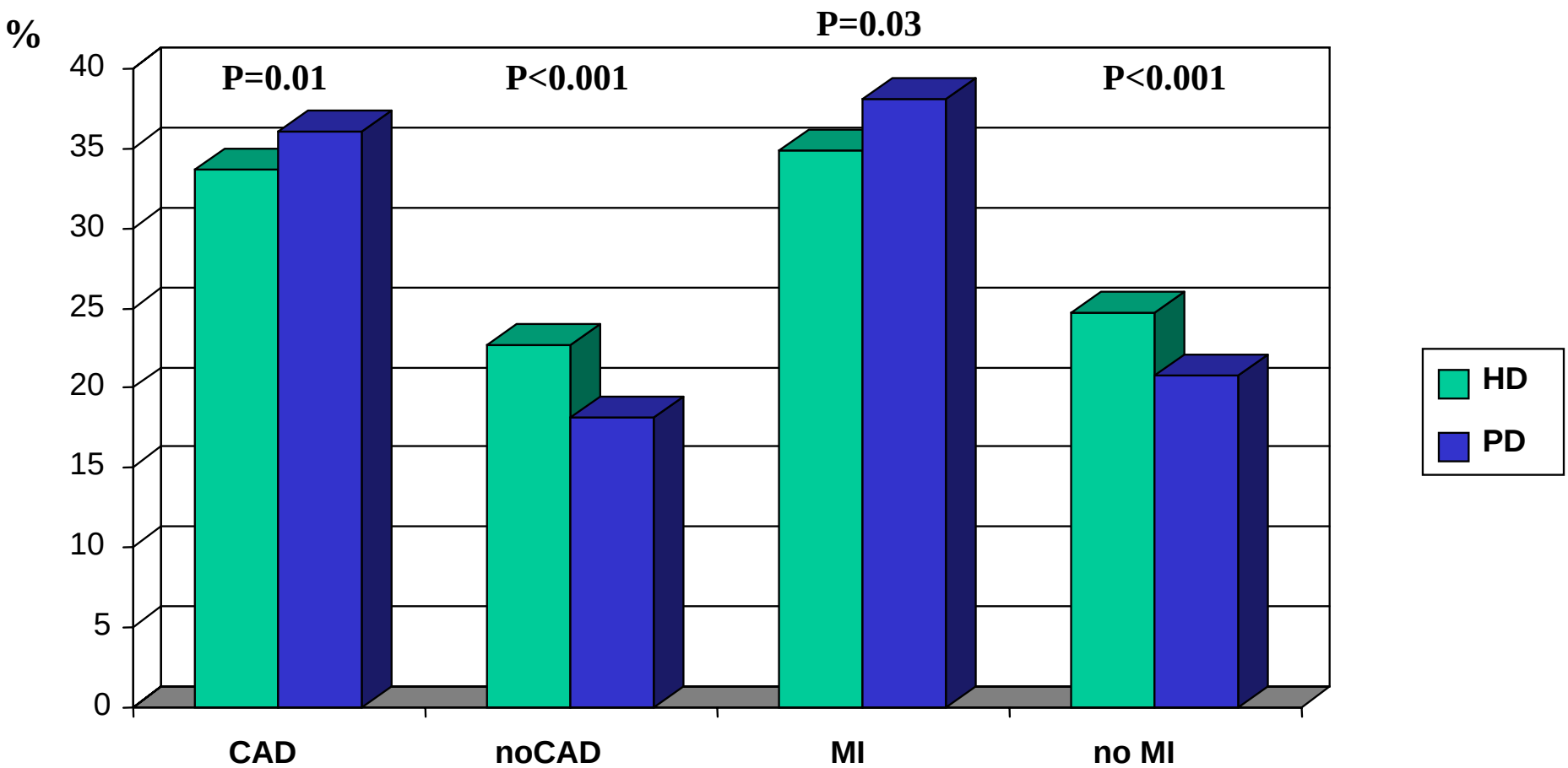
Ishani et al, KI, 2005

Survival in large patients PD vs HD



Abbot et al, KI, 2004

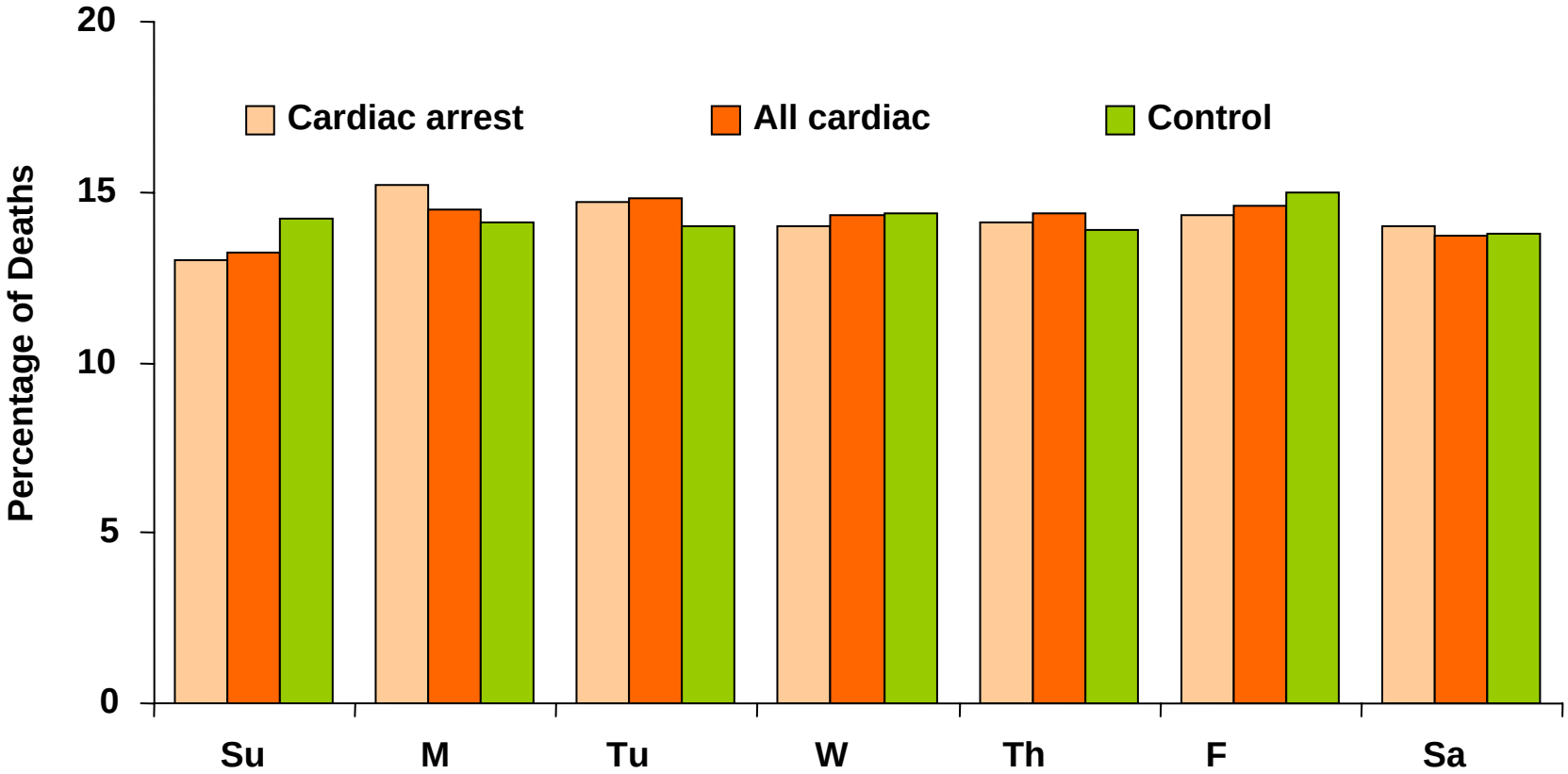
% mortality in USRDS PD (N= 13000) vs HD(N=93000)



Patient inclusion only if survival > 90 days

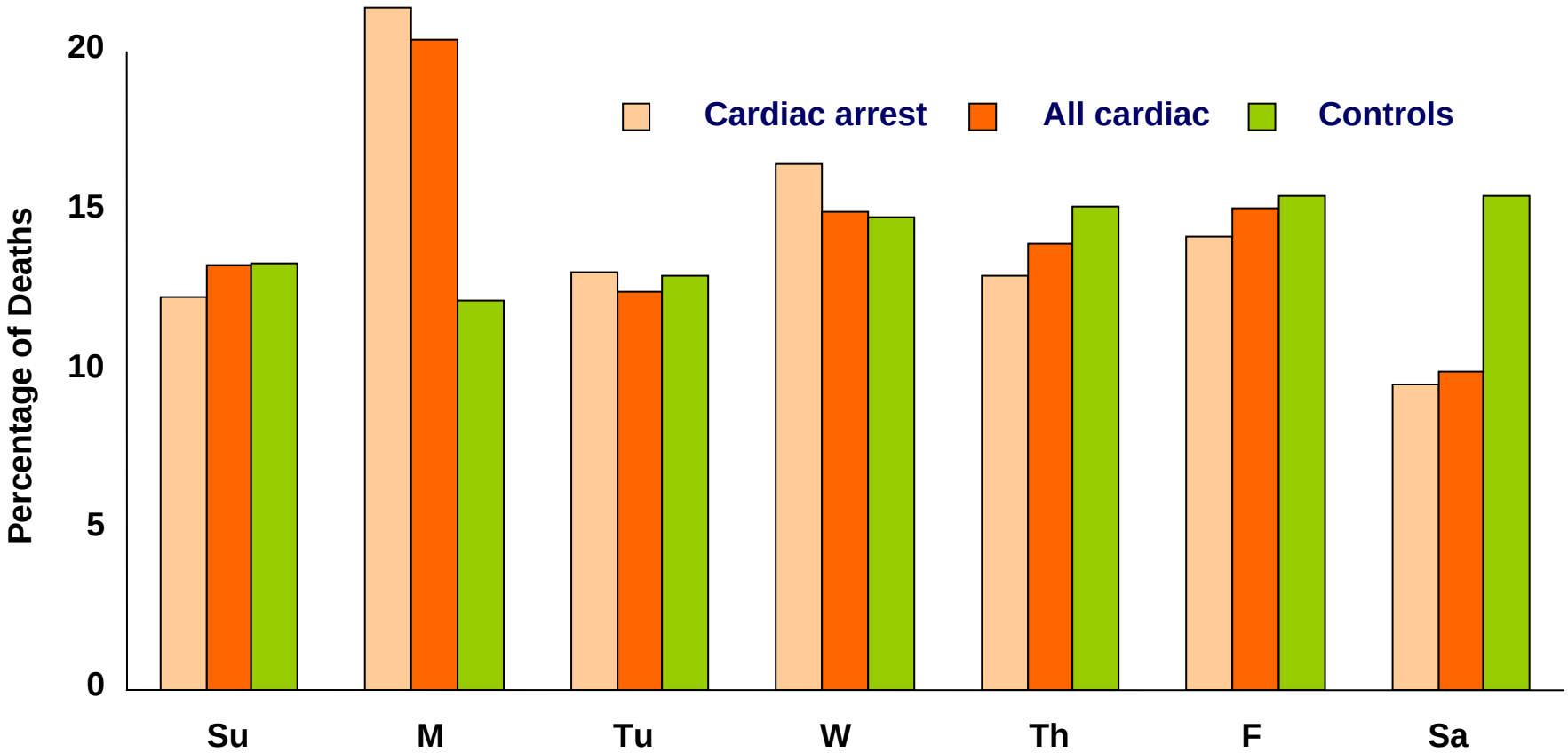
Ganesh et al, JASN, 14, 415-424, 2003

Distribution of Deaths According to Day of the Week for PD Patients



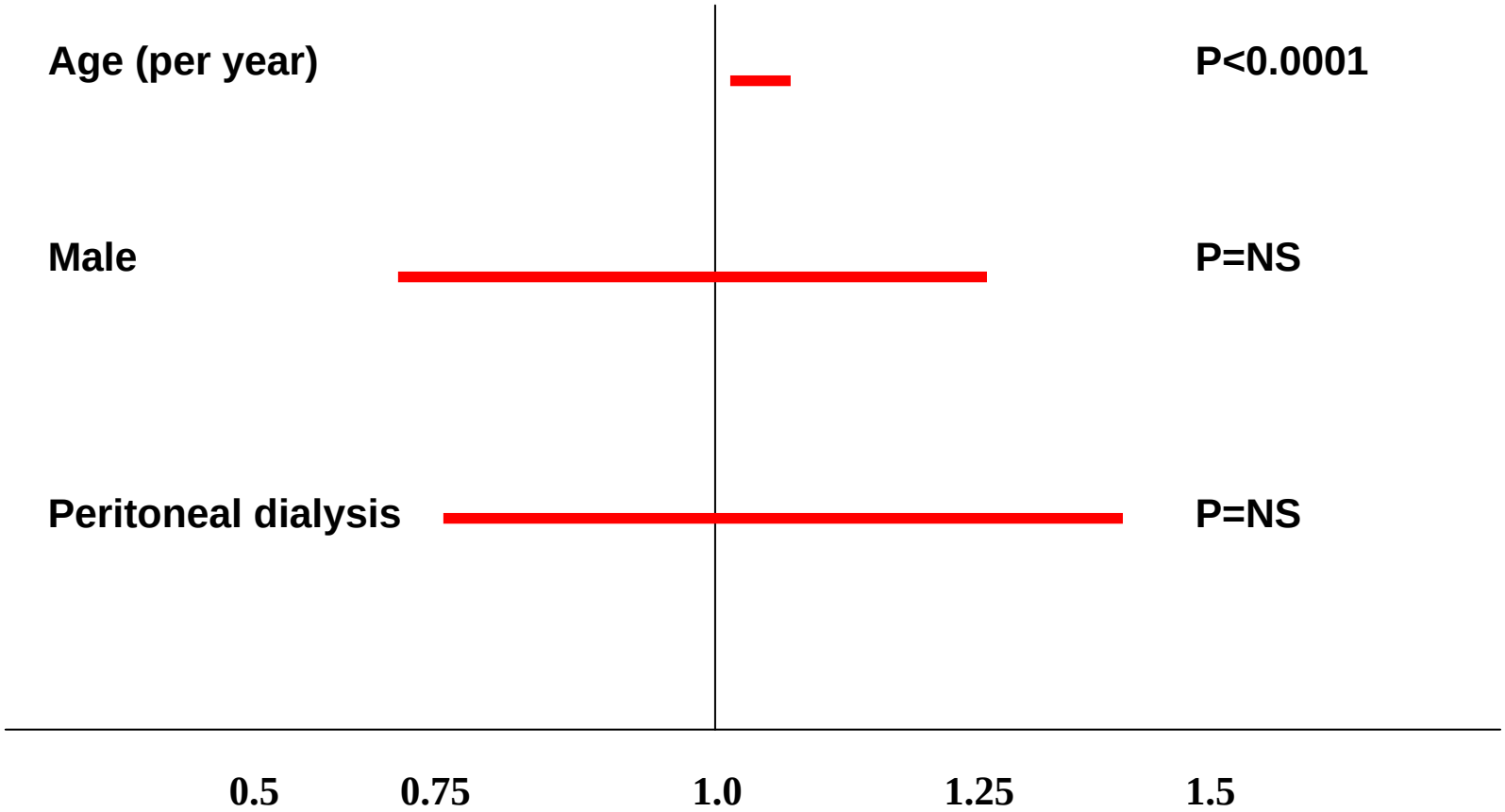
Bleyer AJ, et al, Kidney Int, 1999; 55:1553

Distribution of Deaths According to Day of the Week for M/W/F: HD Patients



Bleyer AJ, et al, Kidney Int, 1999; 55:1553

RR for de novo cardiac disease in RRT patients in Lombardy

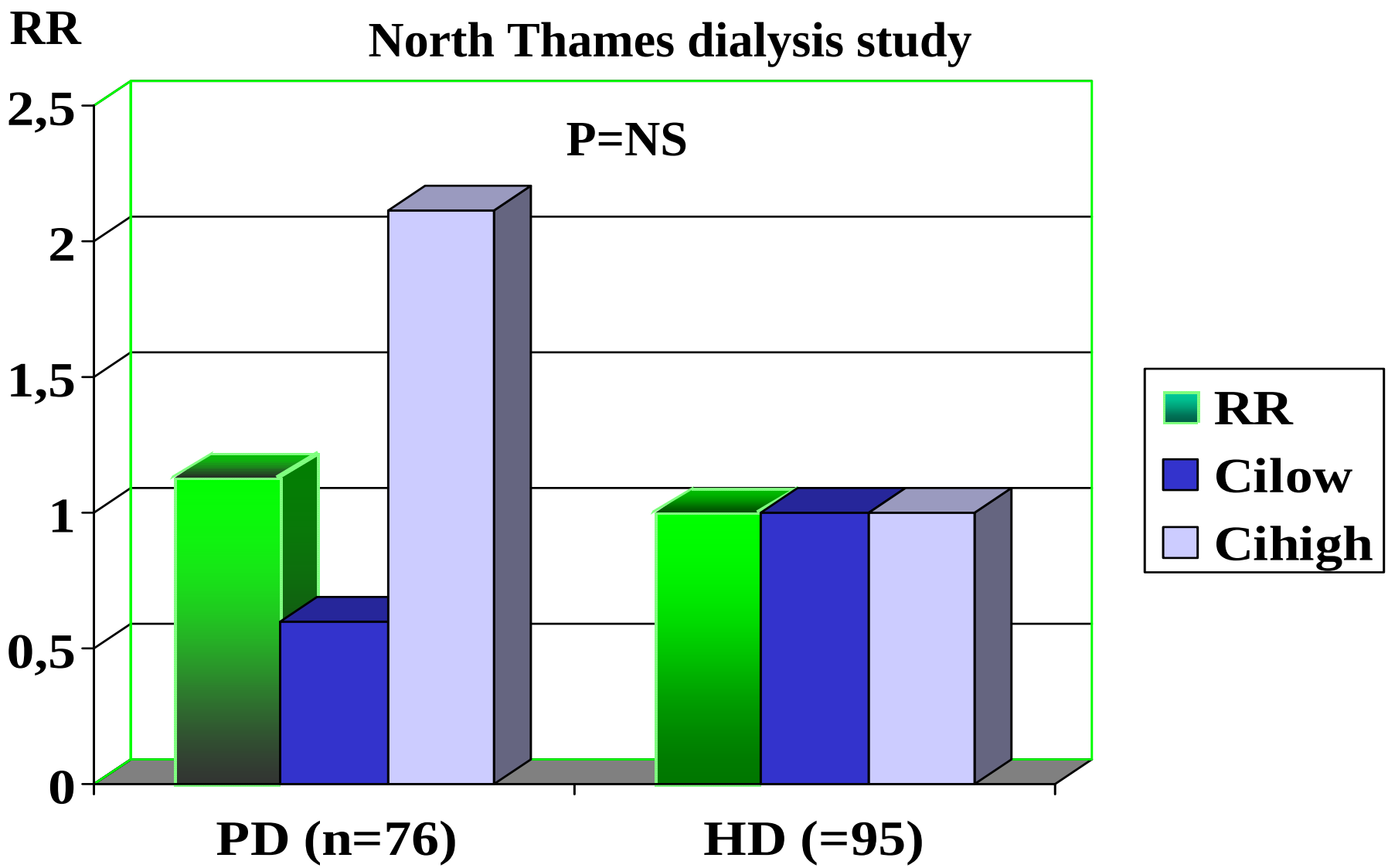


Locatelli et al, JASN, 12, 2411-2417, 2001

Relative advantages and disadvantages of HD and PD in the elderly

	Hemodialysis	Peritoneal dialysis
Advantages	•Long term data available •Suitable for the majority •Independent of patient ability •Manipulation of adequacy •Less time on treatment •Provides social support structure	•No need for vascular access •Less risk of hypotension •Patient independence of hospital •Ease of travel •Maintains residual renal function •Can be done by family member
Disadvantages	•Increased vascular access problems •Increased use of central catheters •Increased risk of sepsis •Increased risk of hypotension •Reliance of transport	•Not suitable in all patients •Increased difficulty in learning •Social isolation •Peritonitis

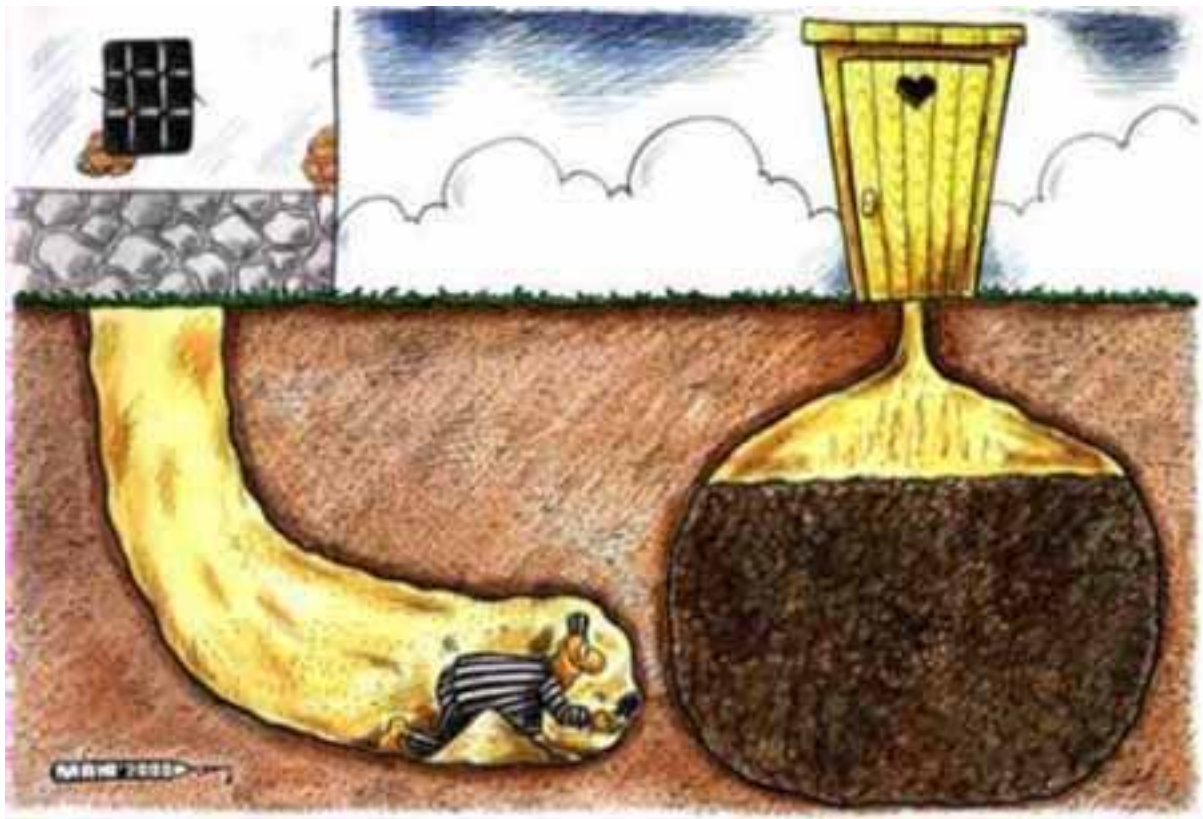
Mortality risk in elderly patients (>70 years)



Harris et al. Perit Dial Int. 2002 Jul-Aug;22(4):463-70

Conclusions

- PD is a simple and efficient treatment
- PD is more than an escape for failed hemodialysis!



Conclusions

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- Take care of volume: salt and water

Conclusions

- PD is a simple and efficient treatment
- More is not always better
- Take care of volume: salt and water
- Look at the patient, not the numbers