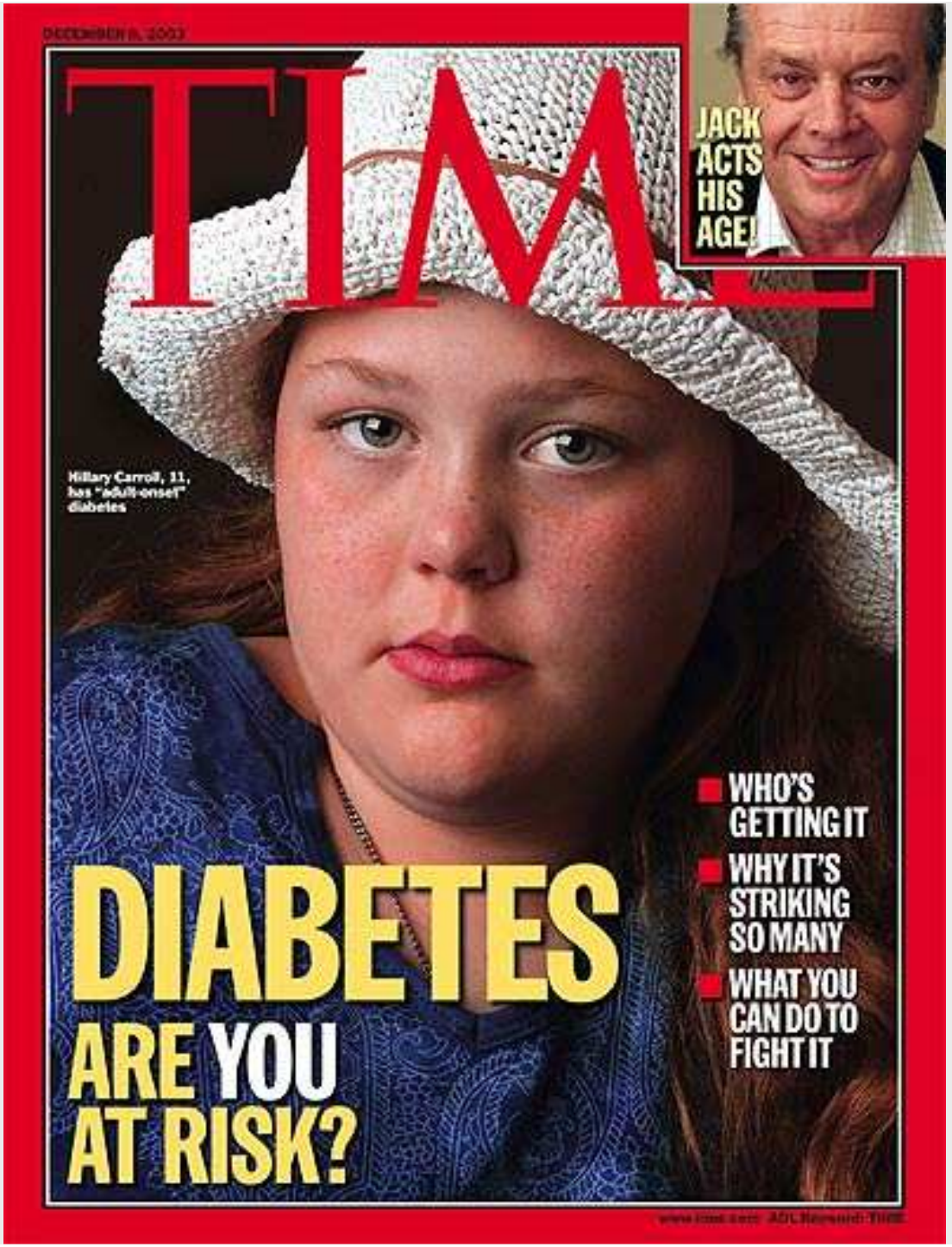
Diabetes and peritoneal dialysis

S. Van Laecke

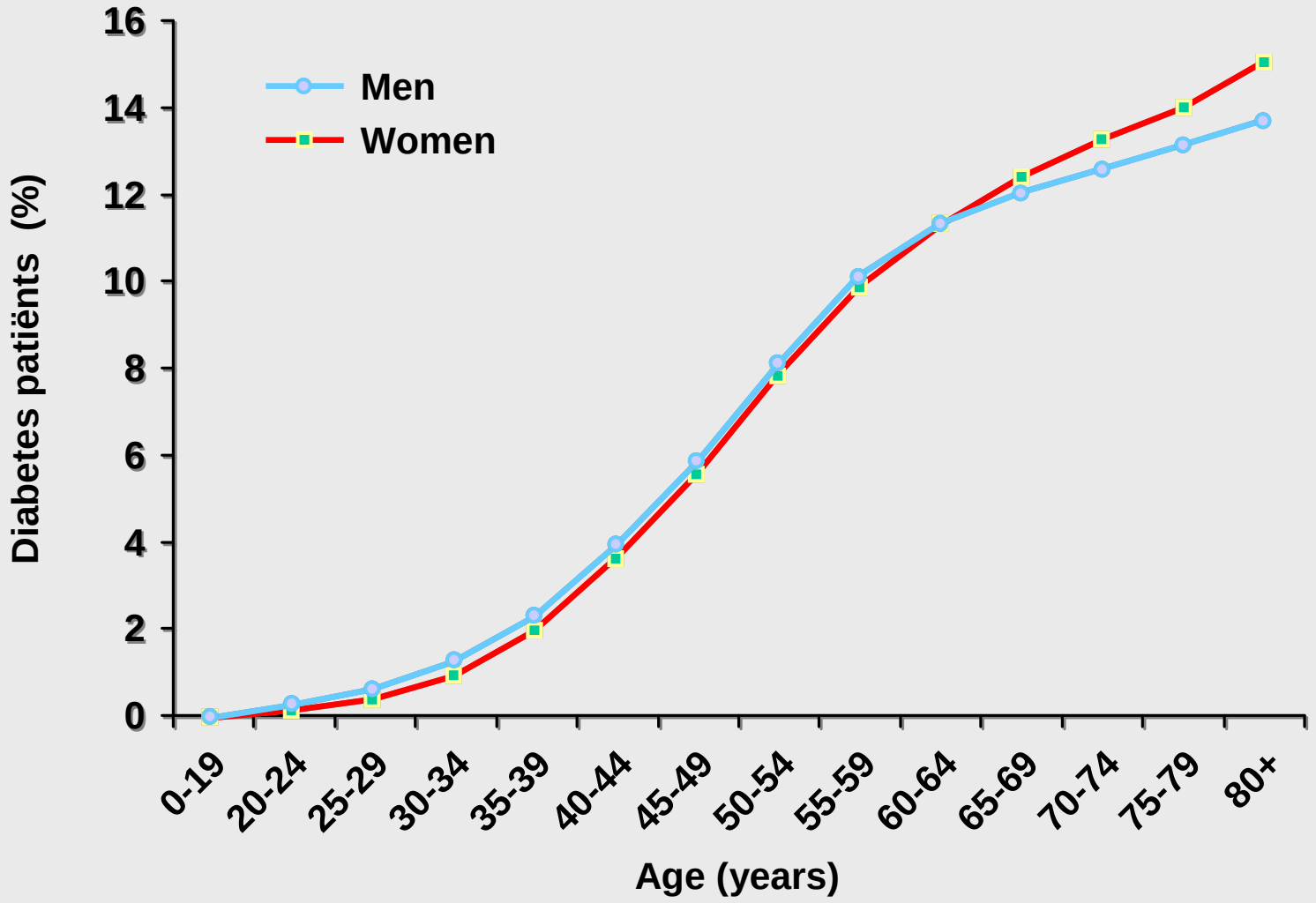
UZ Gent


TIME
JACK ACTS HIS AGE!
Hillary Carroll, 11, has "adult-onset" diabetes
DIABETES
ARE YOU AT RISK?
WHO'S GETTING IT
WHY IT'S STRIKING SO MANY
WHAT YOU CAN DO TO FIGHT IT

Diabetes mellitus: facts

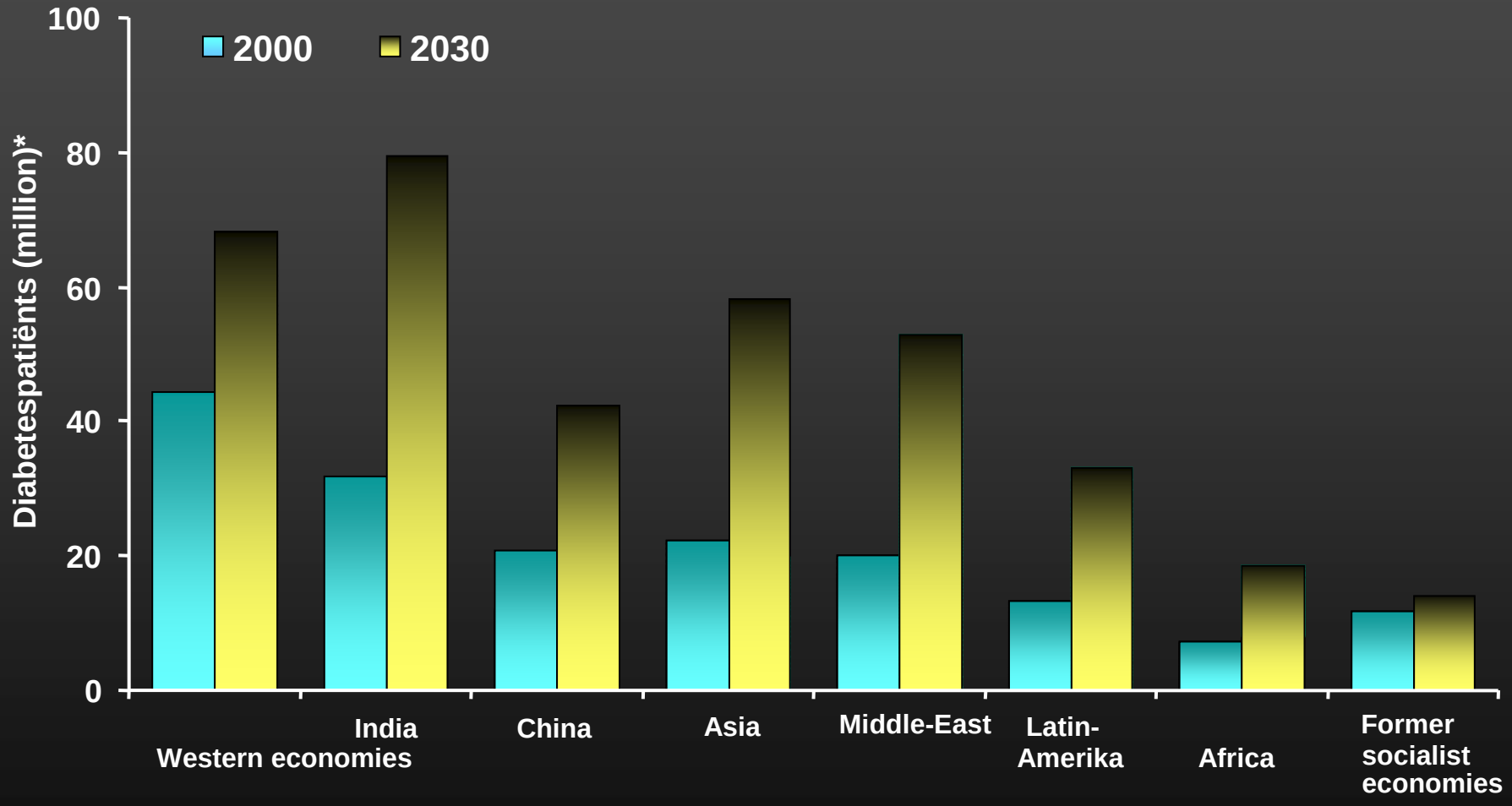
- By the year 2030 366 million people (4,4% vs. 2,8% now)
- Caused by genetic, environmental factors, chronic subclinical inflammation and especially insulin resistance
- Enhanced cardiovascular morbidity and mortality: especially in females
- About one third of the new patients receiving dialysis treatment

Worldwide prevalence of diabetes in 2000 (according to age and sex)



Adapted by Wild S et al. *Diabetes Care.* 2004;27:1047-1053

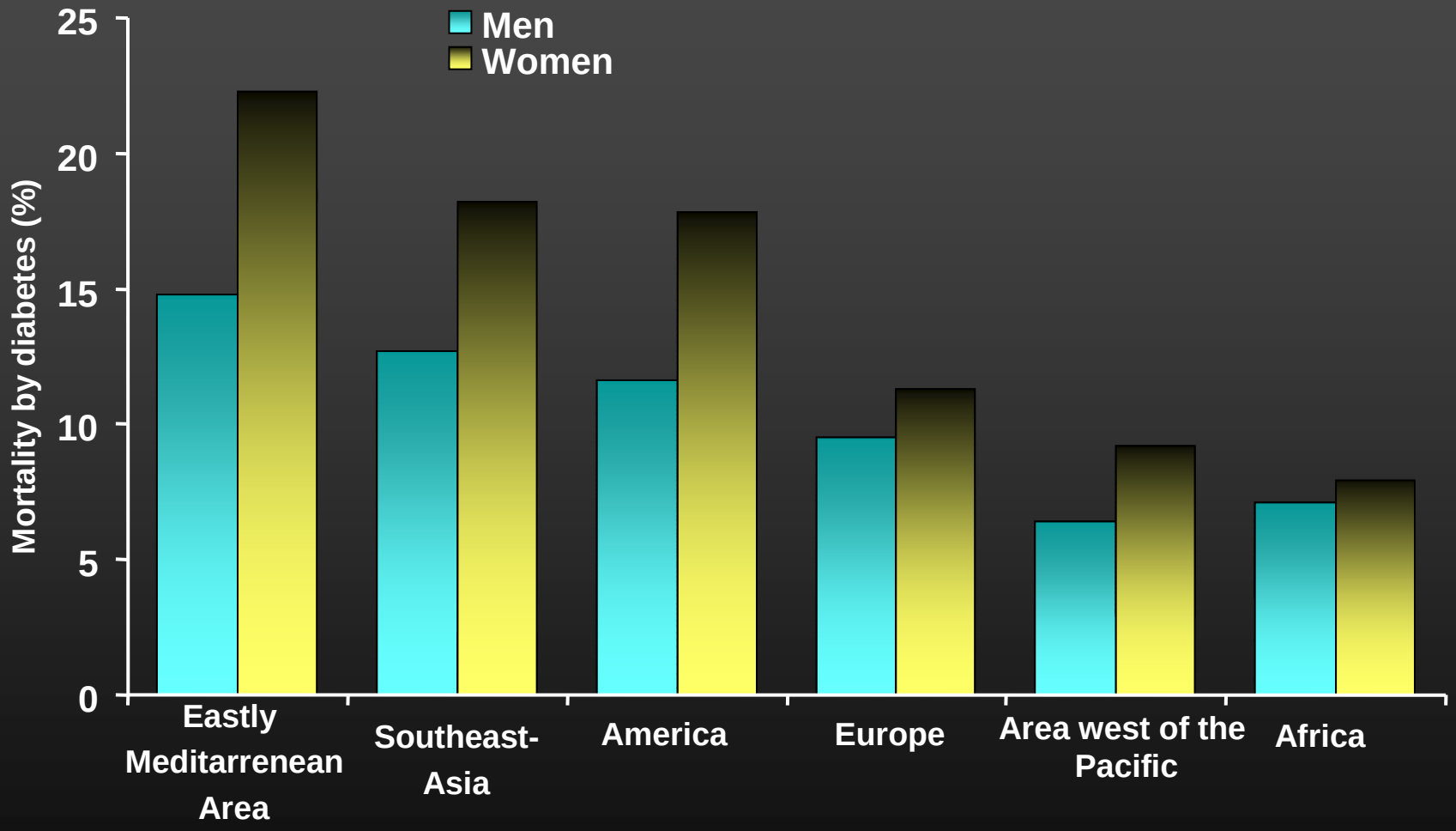
Expectancy of diabetes in 2030



In adullts aged>20y

Wild S et al. *Diabetes Care.* 2004;27:1047-1053

Mortality due to diabetes*

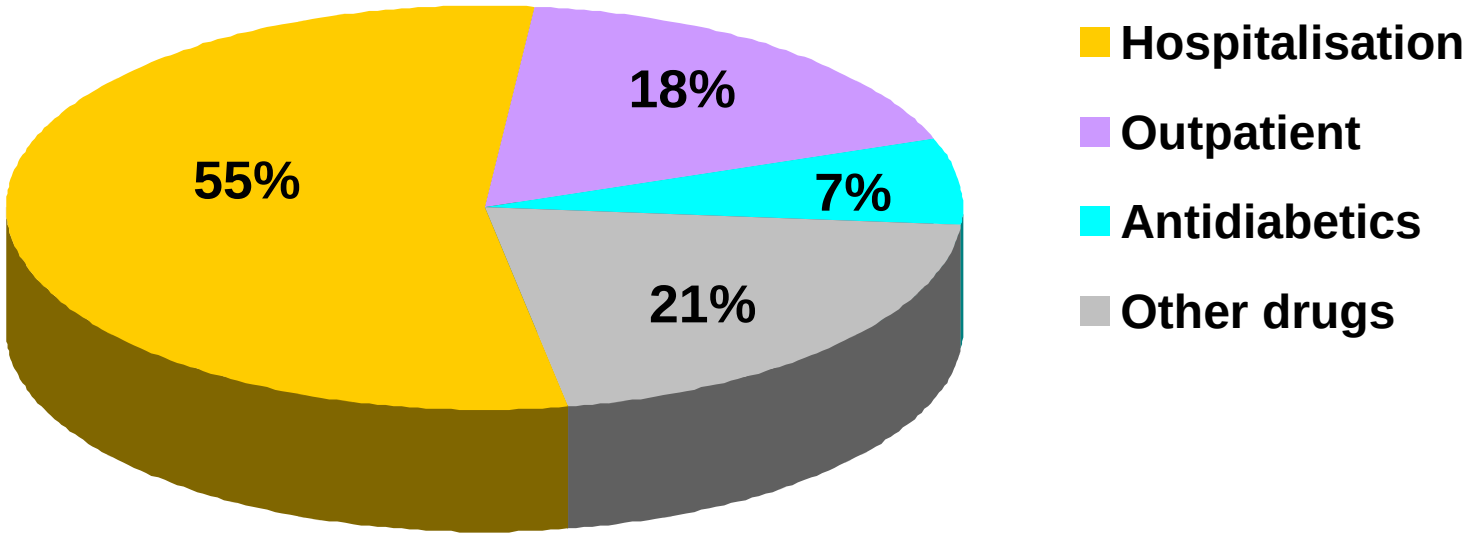


* Adults in 2000 from 35 to 64y

Adapted by Roglic G et al. *Diabetes Care.* 2005;28:2130-2135

Costs of type 2 diabetes in Europe

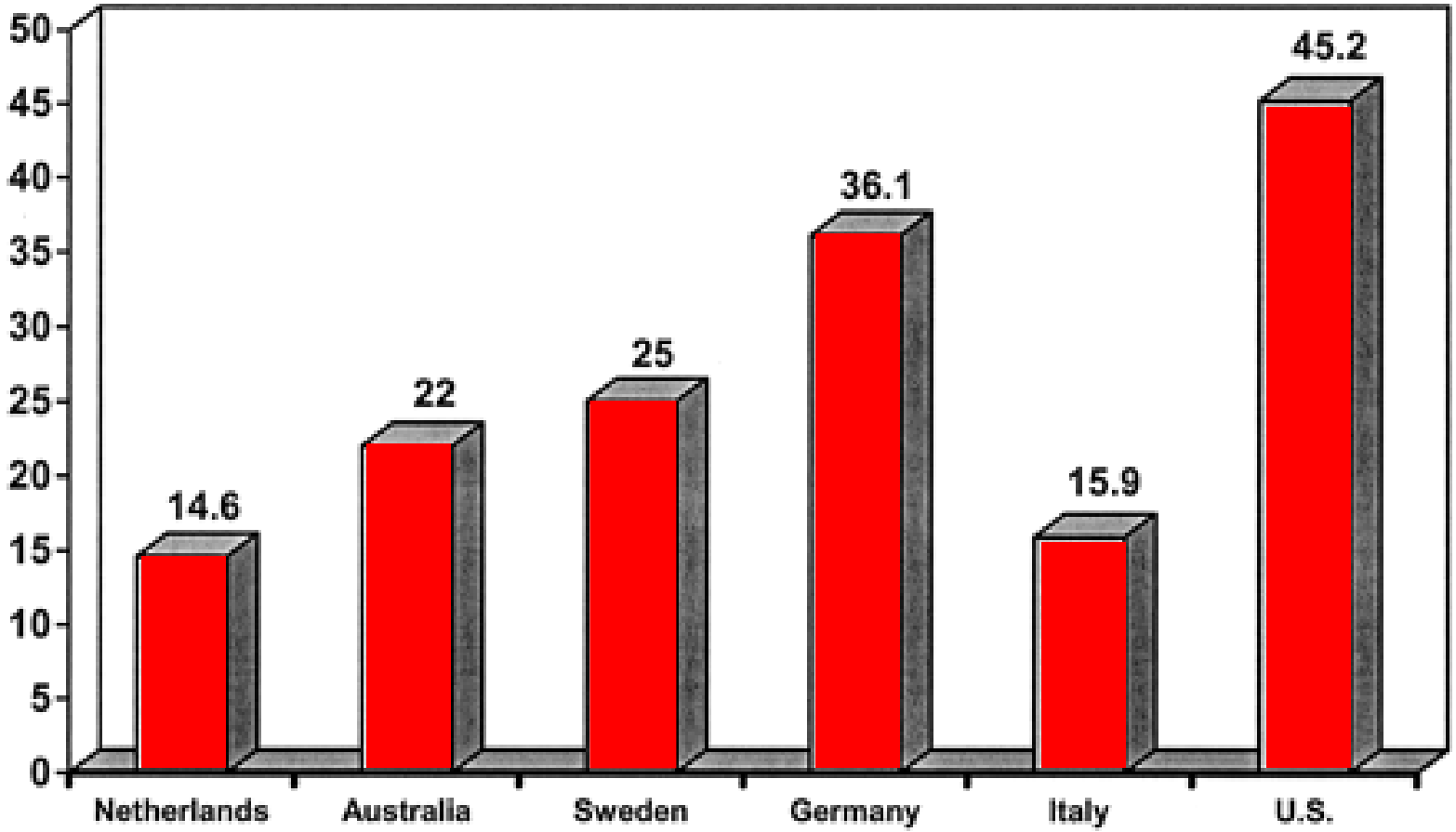
The total direct and estimated costs for diabetes in 7 European countries* were estimated in 1999 on € 28 billion (2.834 € per patiënt)



* Belgium, France, Germany,Italy, the Netherlands, Sweden, the UK

Jönsson B. *Diabetologia.* 2002;45:S5-S12

Diabetes as the primary diagnosis of incident renal replacement treatment patients in 2000

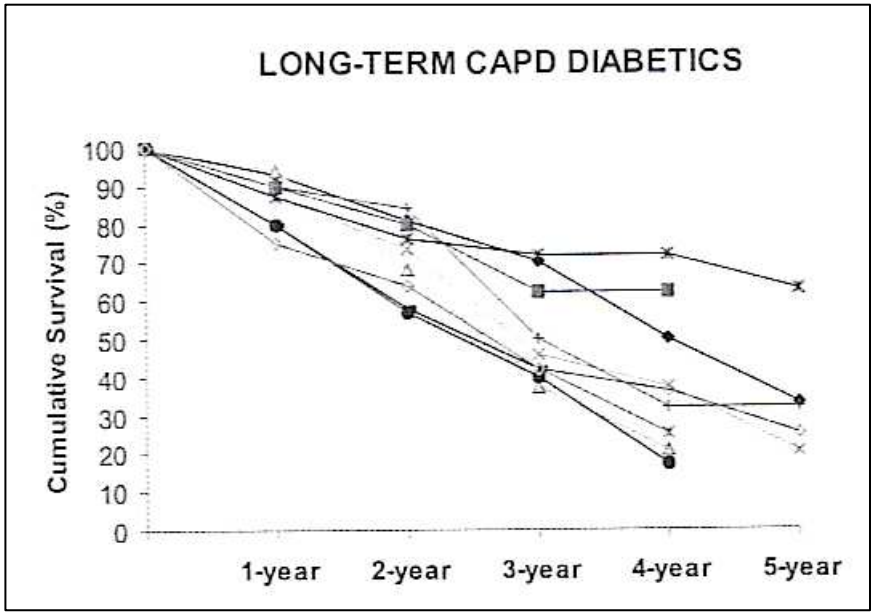


Locatelli F et al. JASON 2004; 15:S25-29

Diabetes mellitus and Peritoneal Dialysis:potential advantages

-no need for vascular access
-no need for systemic anticoagulation
-continuous therapy
-gradual ultrafiltration
-better preservation of renal function
-fewer episodes of hypotension
-better control of anemia
-lifestyle advantages
-more liberal diet

Diabetes mellitus and PD: outcome?



Passadakis P et al. Clinical Nephrology 2001;56:257-70

9 studies

comorbidity?

Diabetes mellitus and PD: outcome

HD better:

USRDS report 2000

Bloembergen et al. JASON 1995:RR 1.38

Held et al. KI 1994:RR 1.34 (>63j)

PD better:

Fenton et al. AJKD 1997:RR 0.73 (0-64j) after adjustment for age,comorbidity

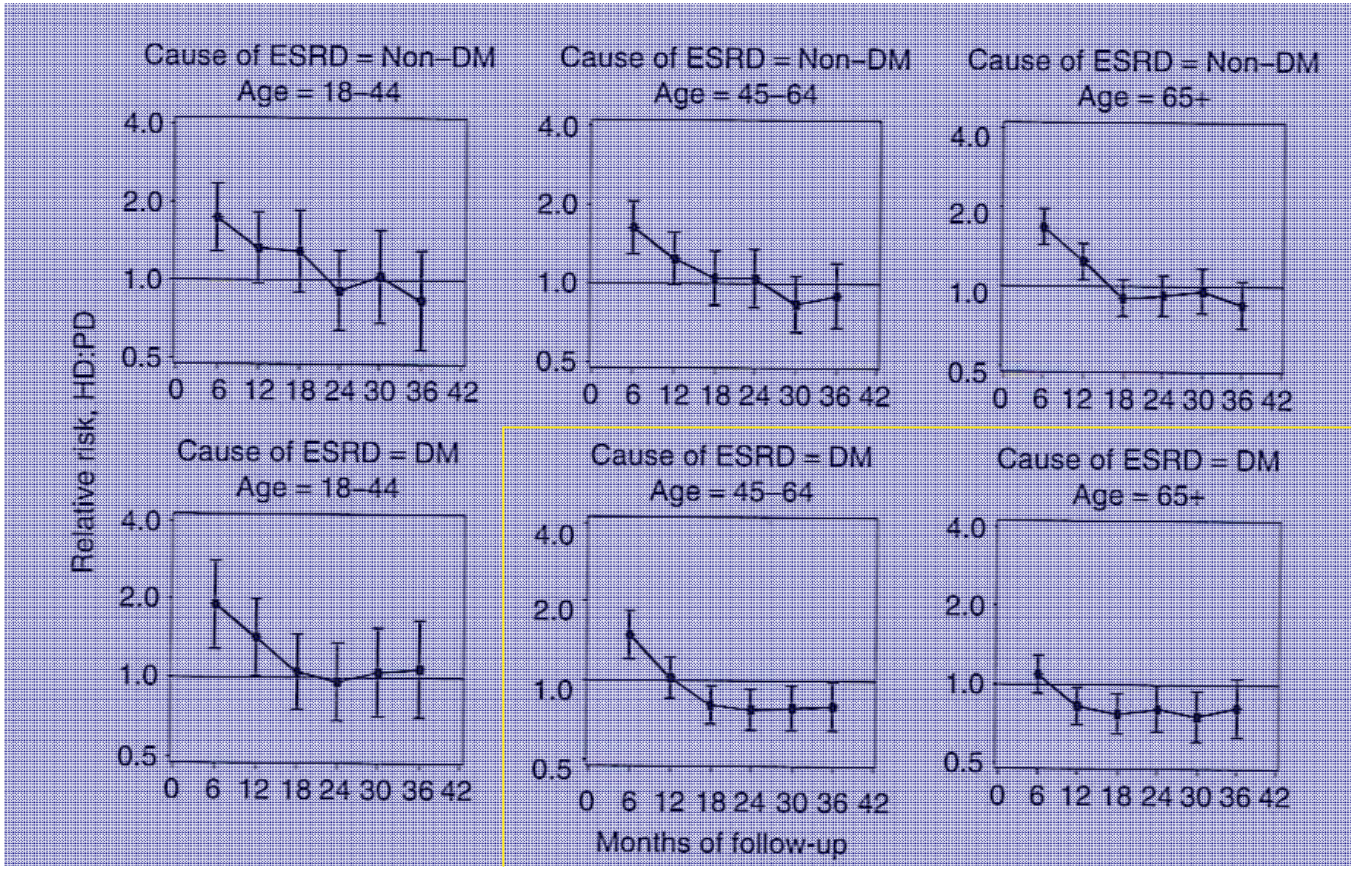
Collins et al. AJKD 1999:RR 1.21 in diabetic women>55j vs. 1.03 in older diabetic men, 0.88 and 0.86 in women and men of <55j resp.

Vonesh et al. JASON 1999 lower risk in PD group except female diabetics

Liem et al. KI 2007 except for older diabetics

More **technique failure in diabetics** versus non-diabetics *(JASON 2000, Van Biesen et al*) with RR 1.81 ($p<0.001$) and versus HD (RR 1.39 with $p<0.02$)

Survival in HD versus PD

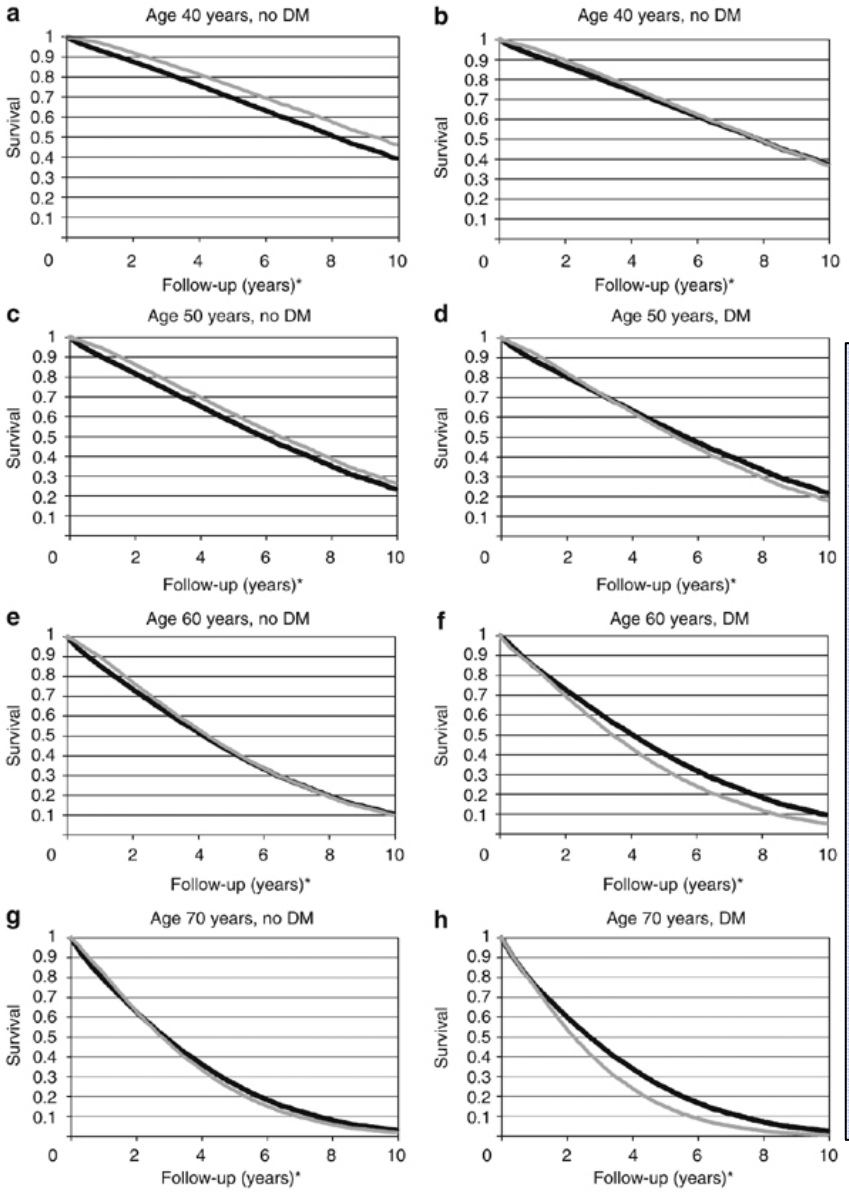


Vonesh et al. KI 2004;66:2389-2401

http://www.kidney-international.org original article

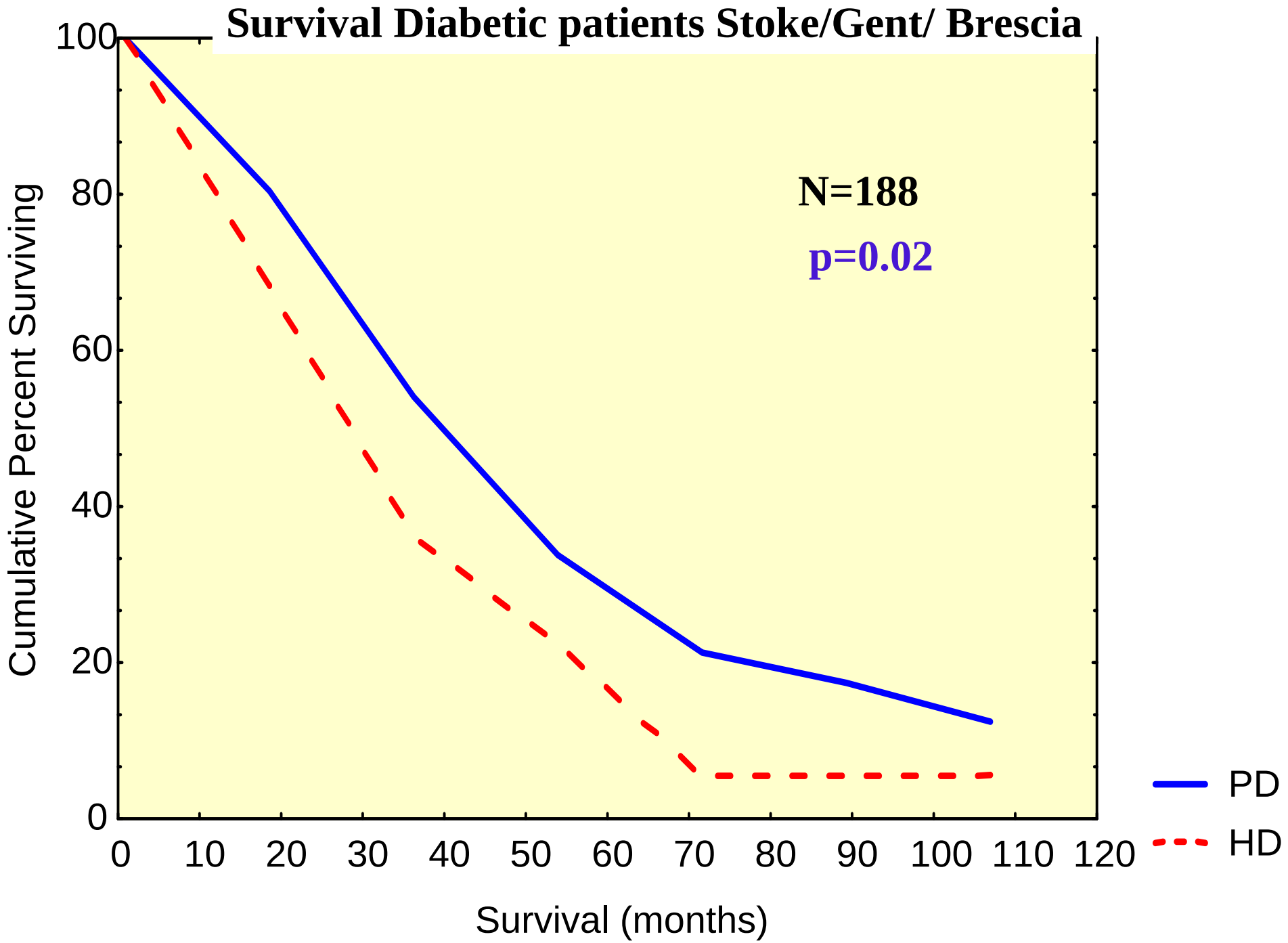
Comparison of hemodialysis and peritoneal dialysis survival in The Netherlands

YS Liem[1,2,3], JB Wong[4], MGM Hunink[1,2,5], FTh de Charro[6] and WC Winkelmayer[7]



Age	DM	HRs of PD vs HD (95% CIs)[a] >3–6 months	>6–15 months	>15 months
40	No	0.26 (0.17; 0.41)	0.51 (0.39; 0.68)	0.86 (0.74; 1.00)
40	Yes	0.40 (0.23; 0.68)	0.59 (0.44; 0.81)	1.06 (0.88; 1.26)
50	No	0.35 (0.25; 0.48)	0.62 (0.51; 0.76)	0.95 (0.85; 1.05)
50	Yes	0.53 (0.34; 0.83)	0.72 (0.56; 0.93)	1.17 (1.00; 1.35)
60	No	0.46 (0.37; 0.58)	0.75 (0.65; 0.87)	1.05 (0.97; 1.13)
60	Yes	0.71 (0.48; 1.04)	0.87 (0.71; 1.09)	1.29 (1.12; 1.48)
70	No	0.62 (0.50; 0.76)	0.92 (0.80; 1.05)	1.16 (1.07; 1.25)
70	Yes	0.95 (0.64; 1.39)	1.07 (0.85; 1.33)	1.42 (1.23; 1.65)

Liem et al. KI 2007


Survival Diabetic patients Stoke/Gent/ Brescia
N=188
p=0.02
Cumulative Percent Surviving
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
90
100
110
120
Survival (months)
PD
HD

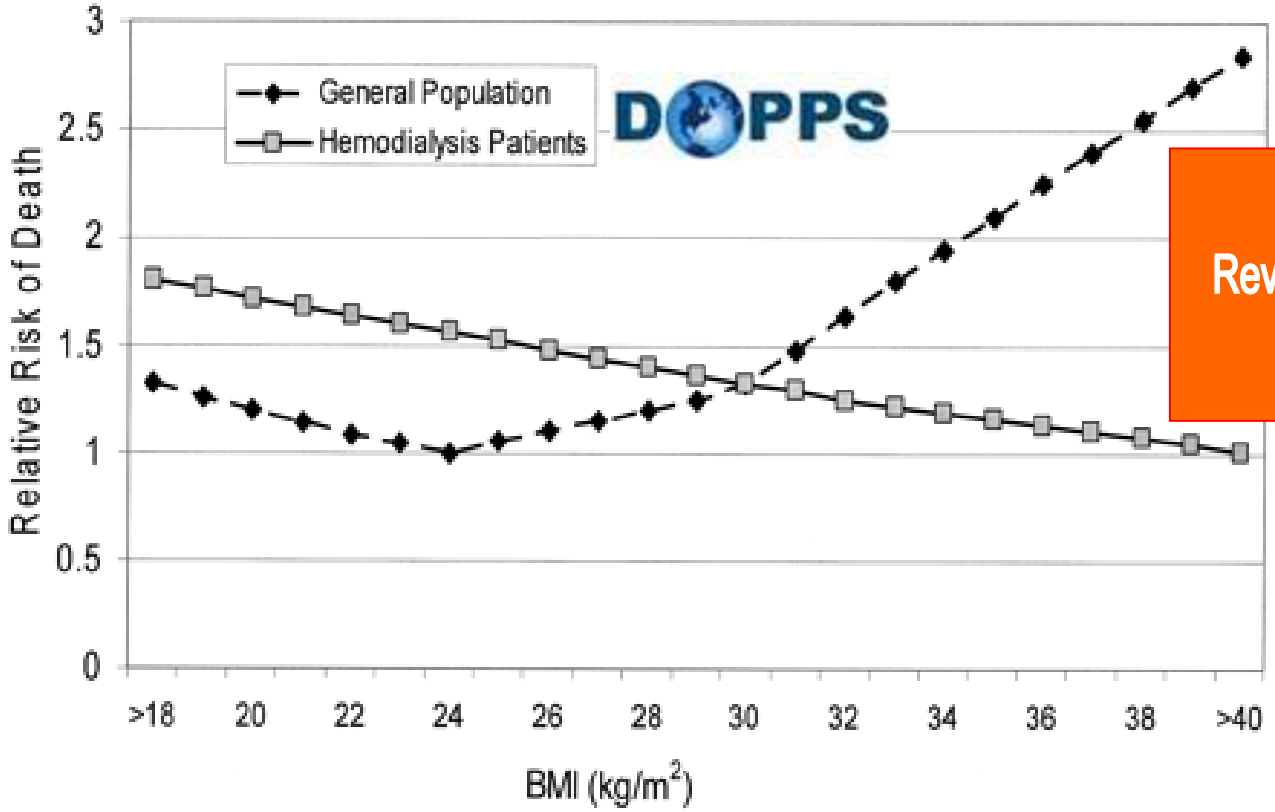
Conclusion (part 1)

- **Caveat bias in US(RDS)-based studies**
- **PD as a first treatment modality might be of benefit for diabetic ESRD patients**
- **Special caution should be given to older female patients**

PD in diabetics: concerns

- Obesity
- Differences in peritoneal membrane structure?
- Impact of glucose loading?
- Higher peritonitis rates?
- Insulin IP or SC?

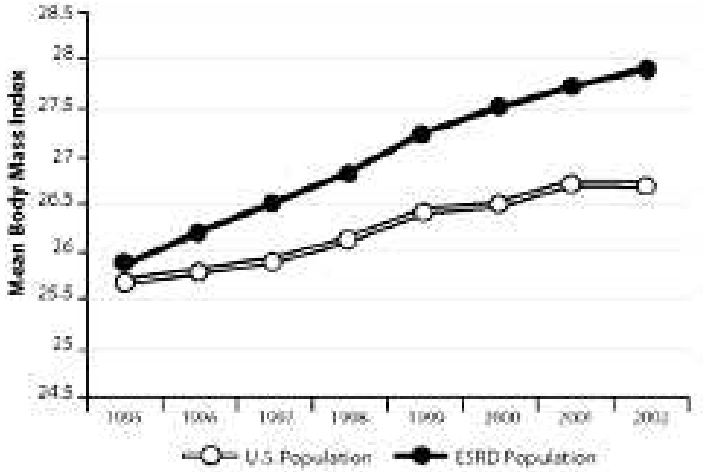
Diabetes mellitus and PD:determinants of survival: the role of obesity

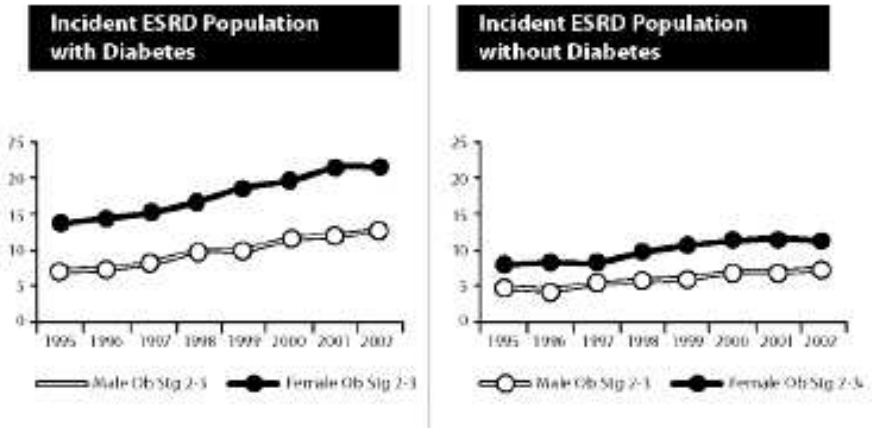


Reverse epidemiology

Leavey SF et al. NDT 2001:16:2386-94

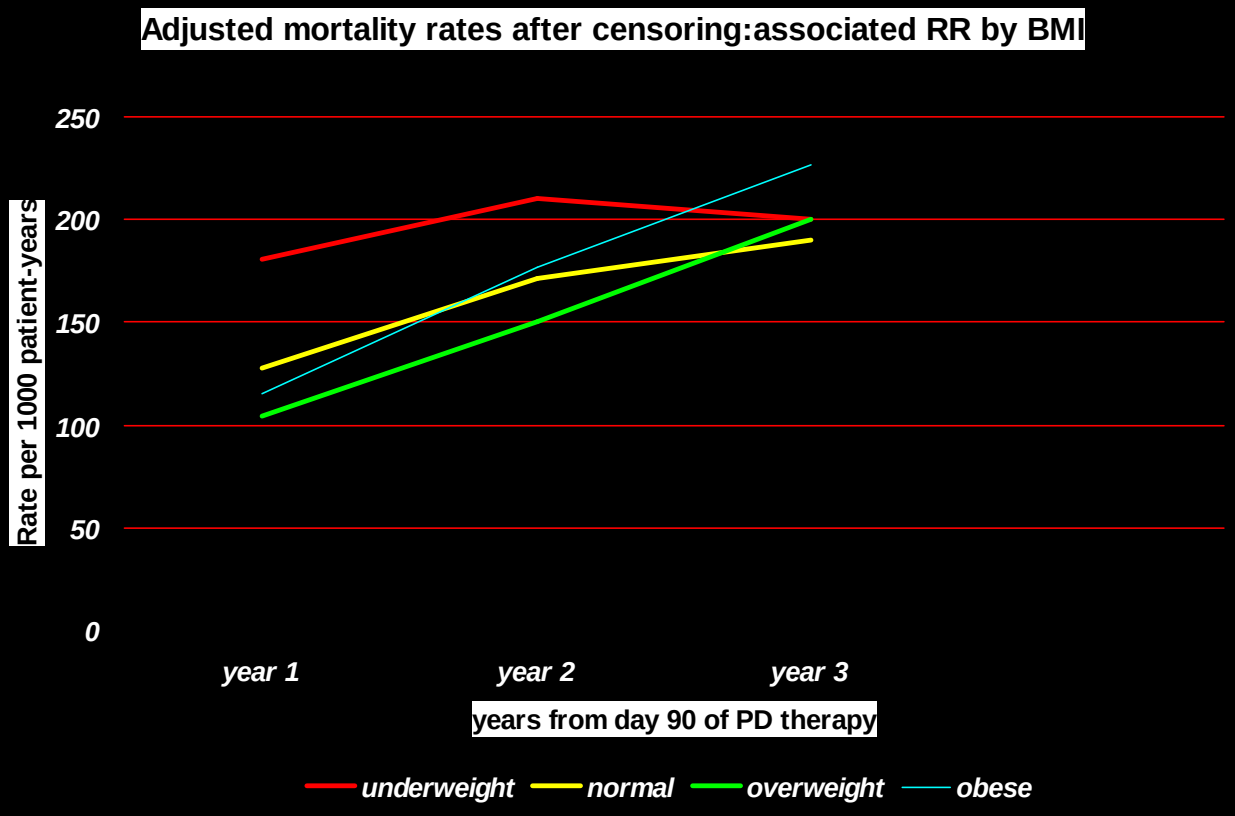
Trends in obesity in the ESRD population





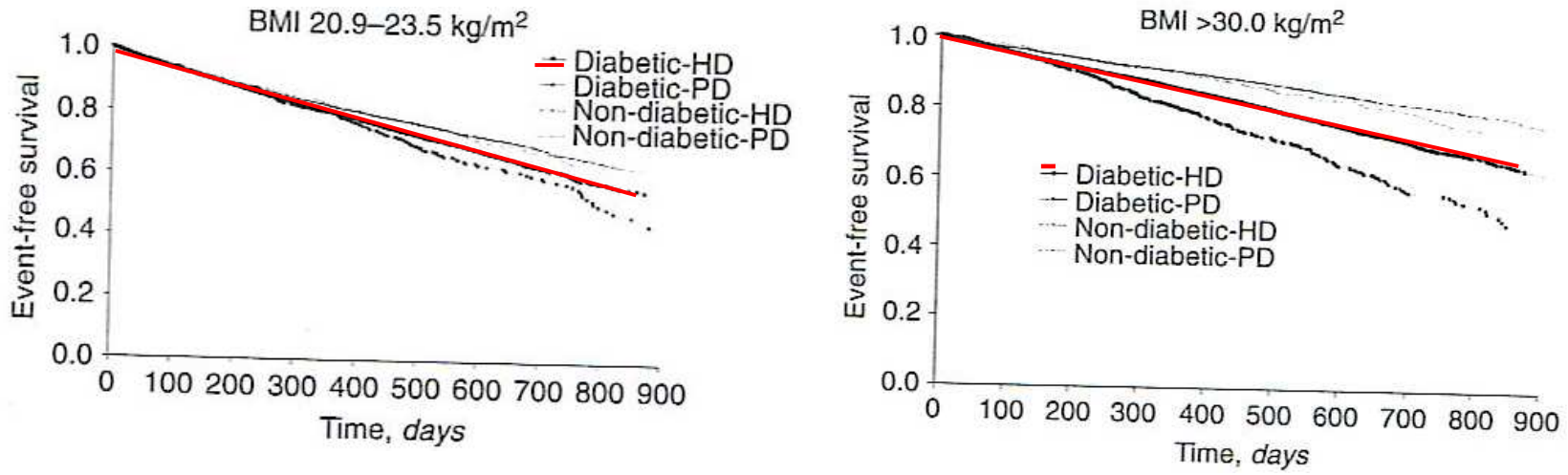
Kramer, JASON 2006;17:1453-59

Diabetes mellitus and PD:determinants of survival: the role of obesity



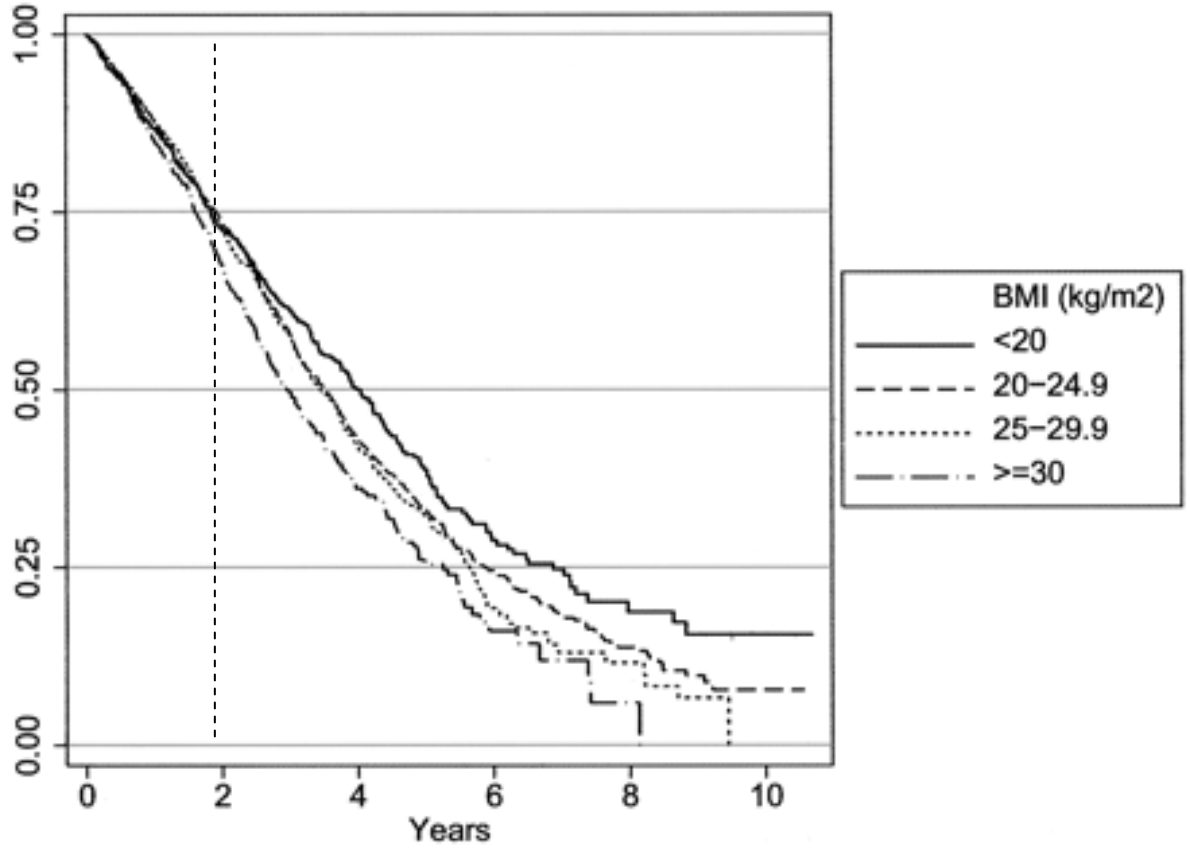
Snyder JJ et al. KI 2003;64:1838-44

Adjusted survival rates for new ESRD patients treated with PD versus HD



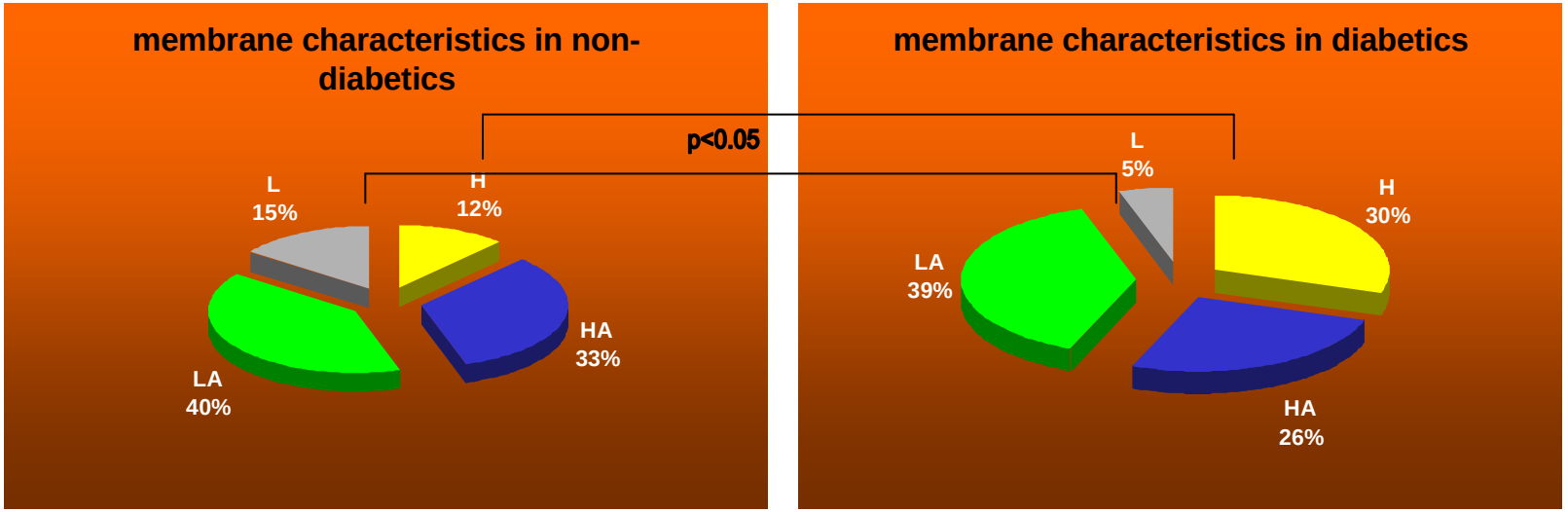
Stack et al. KI 2004;65:2398-2304

Diabetes mellitus and PD:determinants of survival: the role of obesity



McDonald SP. JASON 2003;23:79-83

Diabetes and peritoneal membrane characteristics



Correa-Rotter, PDI 2001;S3:S75-79

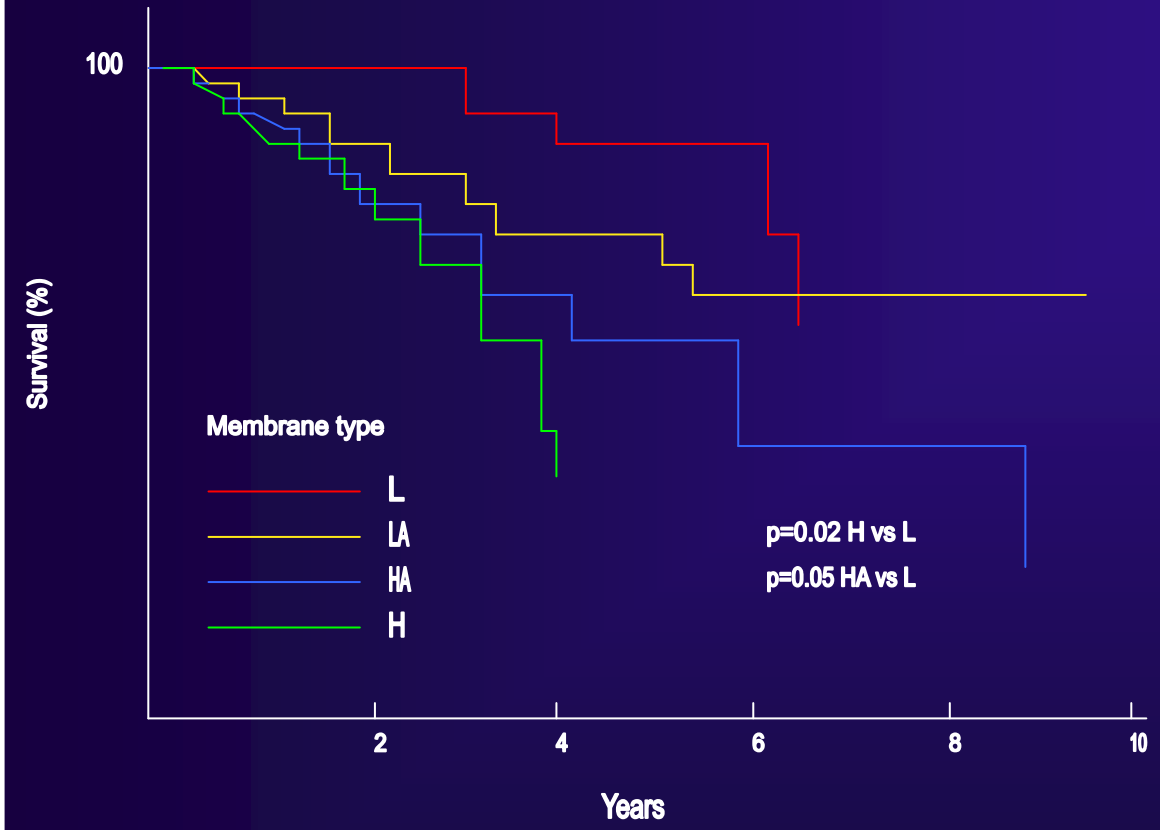
Mind!

Protein losses

Fluid overload

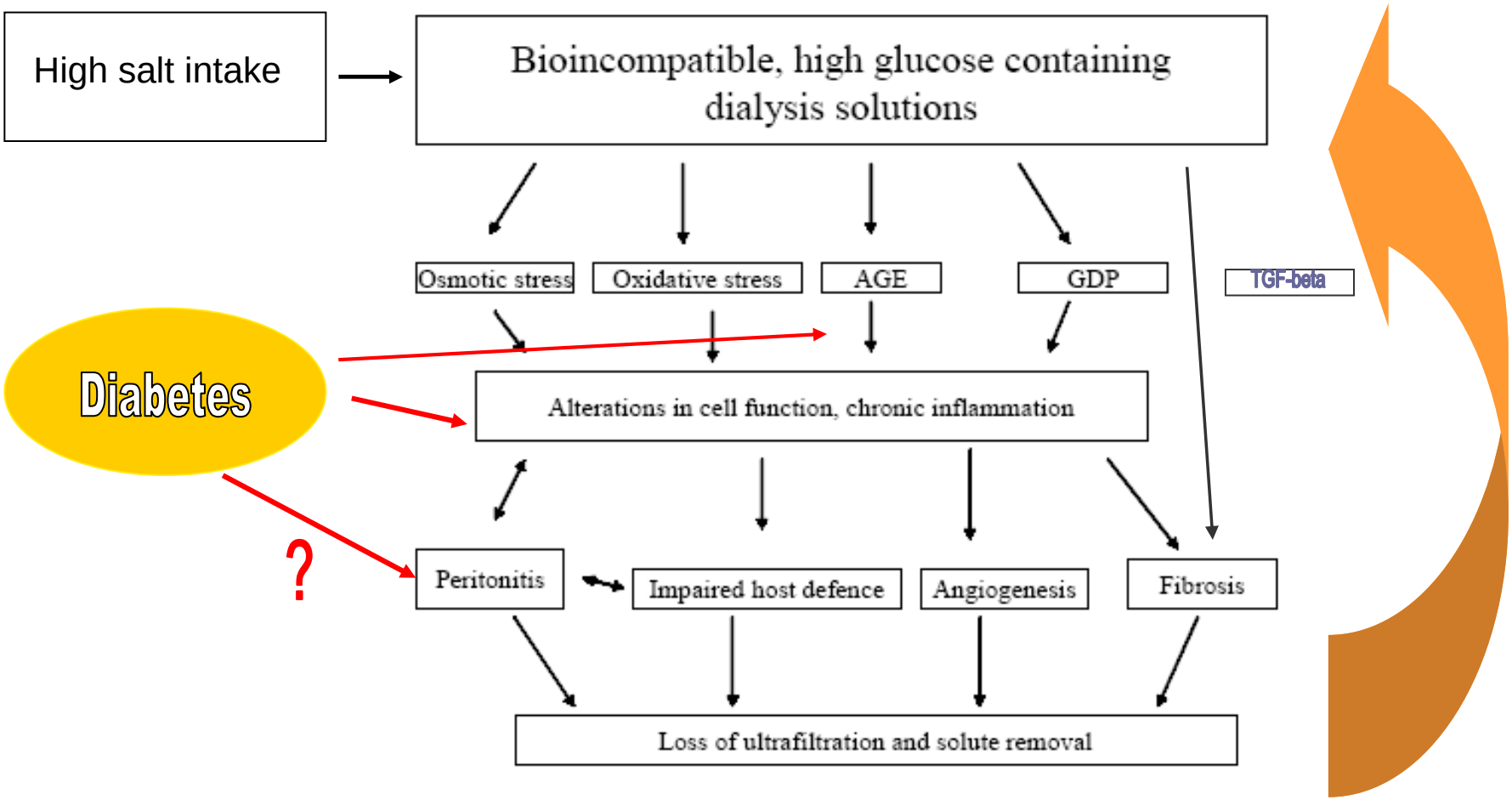
Glucose absorption

Diabetes and peritoneal membrane characteristics



Correa-Rotter, PDI 2001;S3:S75-79

Diabetes mellitus and PD:determinants of survival: the role of inflammation??



<u>Changing peritoneal membrane</u>: after several months on PD: thickening of basal membrane in 26% of diabetics versus 5.6% of non-diabetics

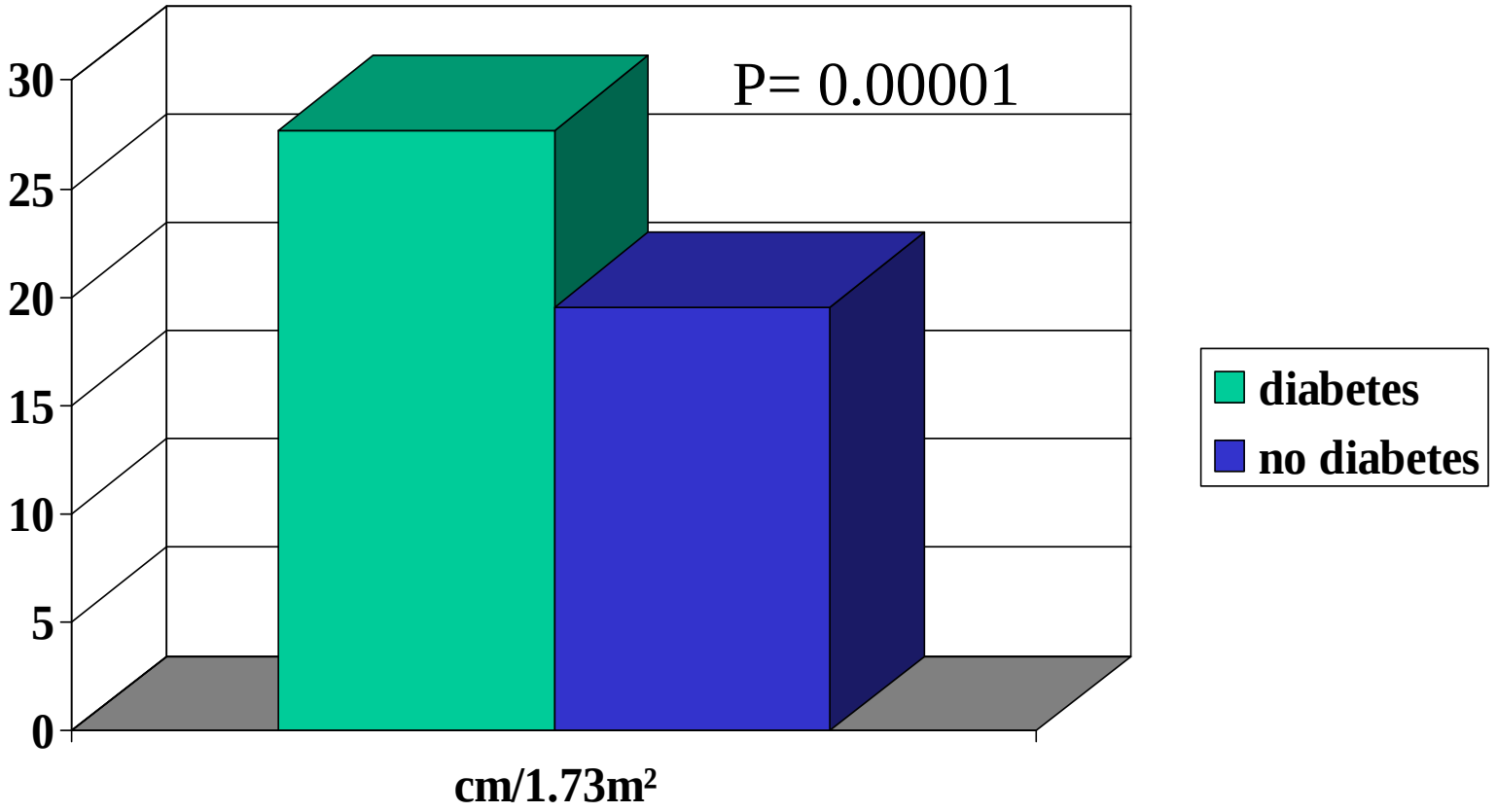
Diabetes mellitus and PD:determinants of survival: the role of inflammation

Glucose Degradation Products (GDPs) Identified in Peritoneal Dialysis Solutions

GDP	Concentration (µmol/L)
Acetaldehyde	120–420
Formaldehyde	6–15
2-Furaldehyde	0.05–2
Glyoxal	3–14
5-Hydroxymethyl furaldehyde	6–30
Methylglyoxal	2–23
Valeraldehyde	ND
3-Deoxyglucosone	118–154
3,4-Dideoxyglucosone-3-ene	9–22

Sitter T. PDI 2005;25:415-25

PDC- Surface area diabetics vs non diabetics



Nakamoto et al, AJKD, 2002

PDC- parameters

Diabetic patients probably

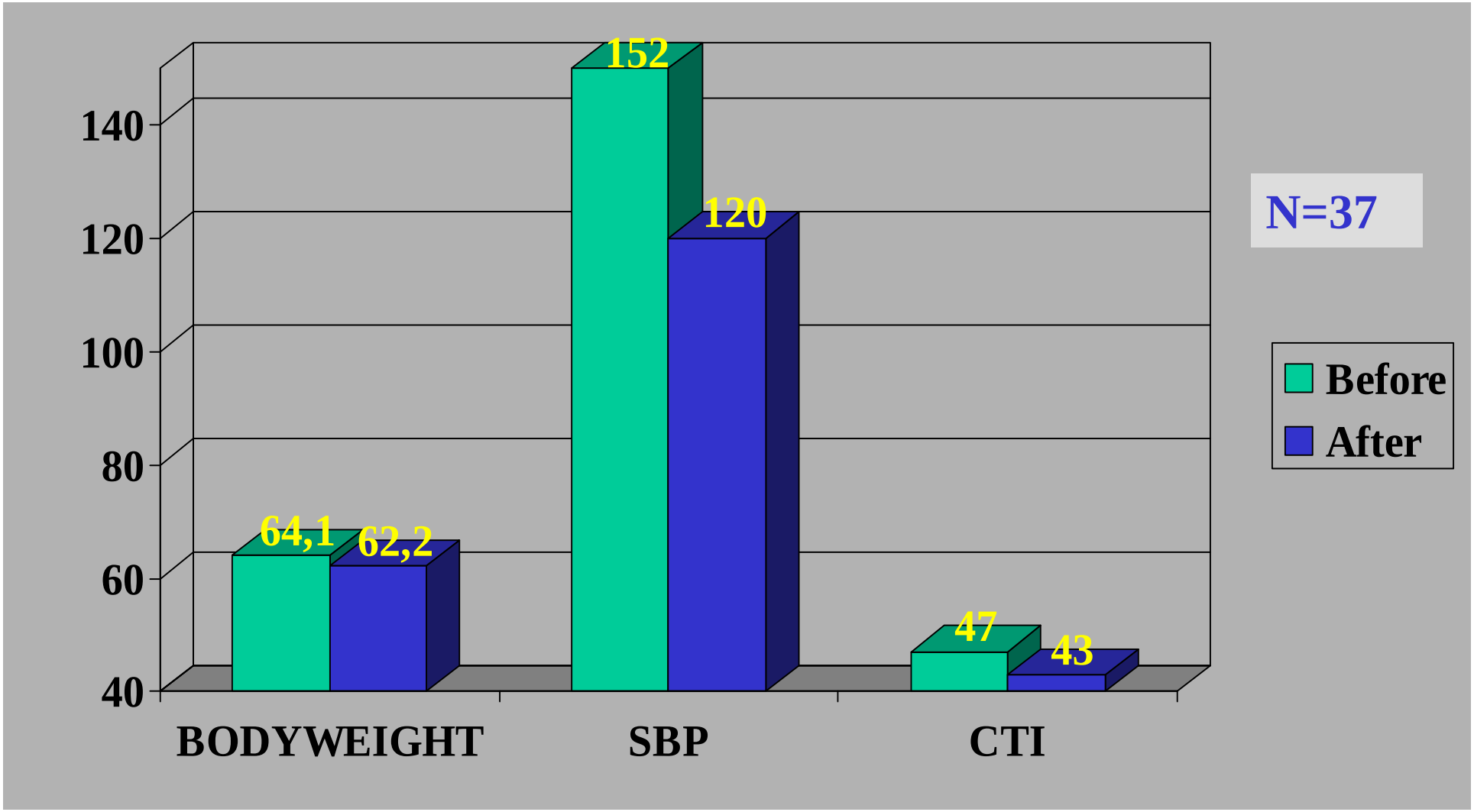
•have a larger vascular surface area, potentially related to neo-angiogenesis

•have a more leaky membrane, probably due to interstitial damage

*multiplied by 10

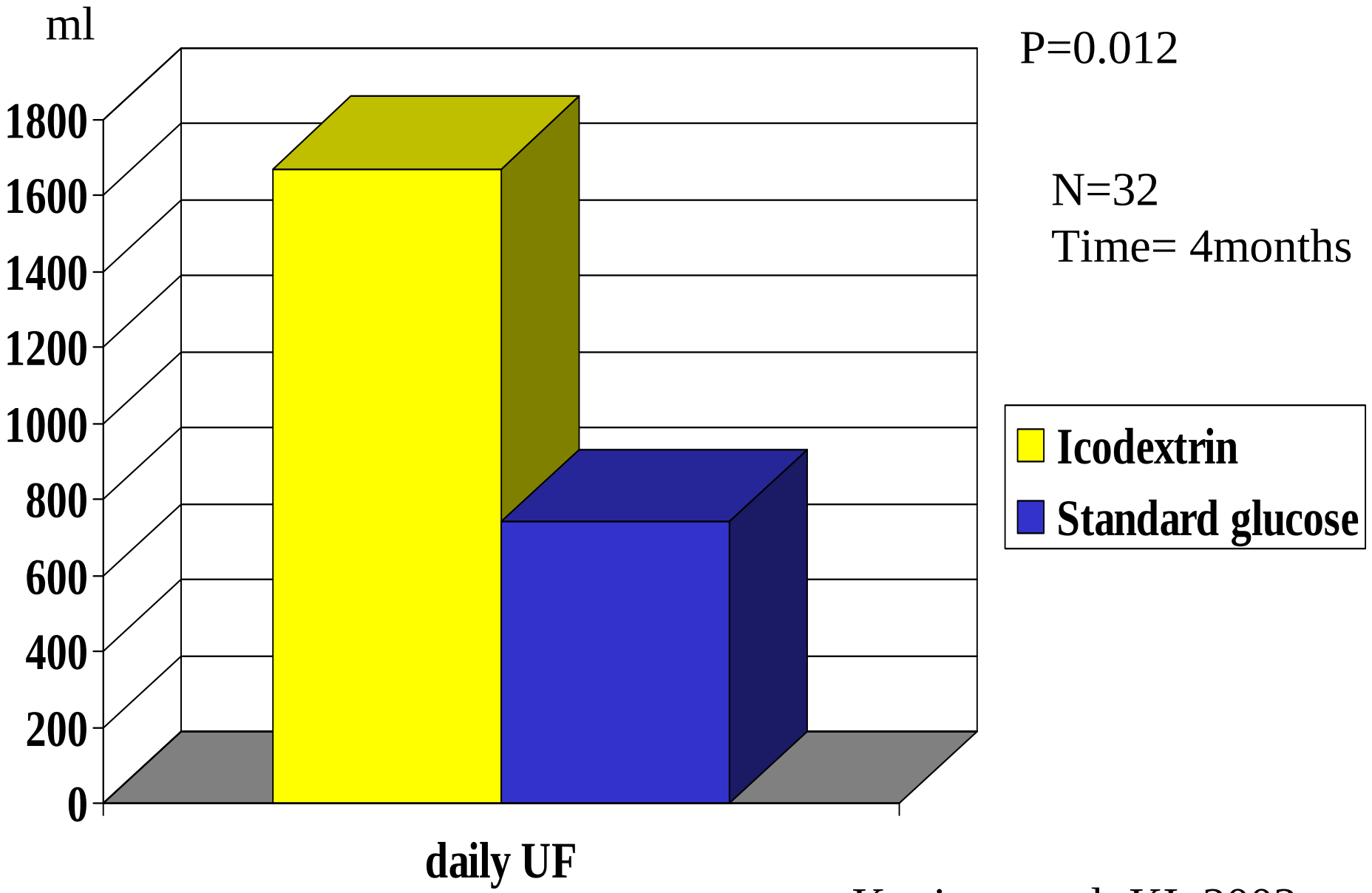
Nakamoto et al, AJKD, 2002

Impact of dietary instructions on salt intake



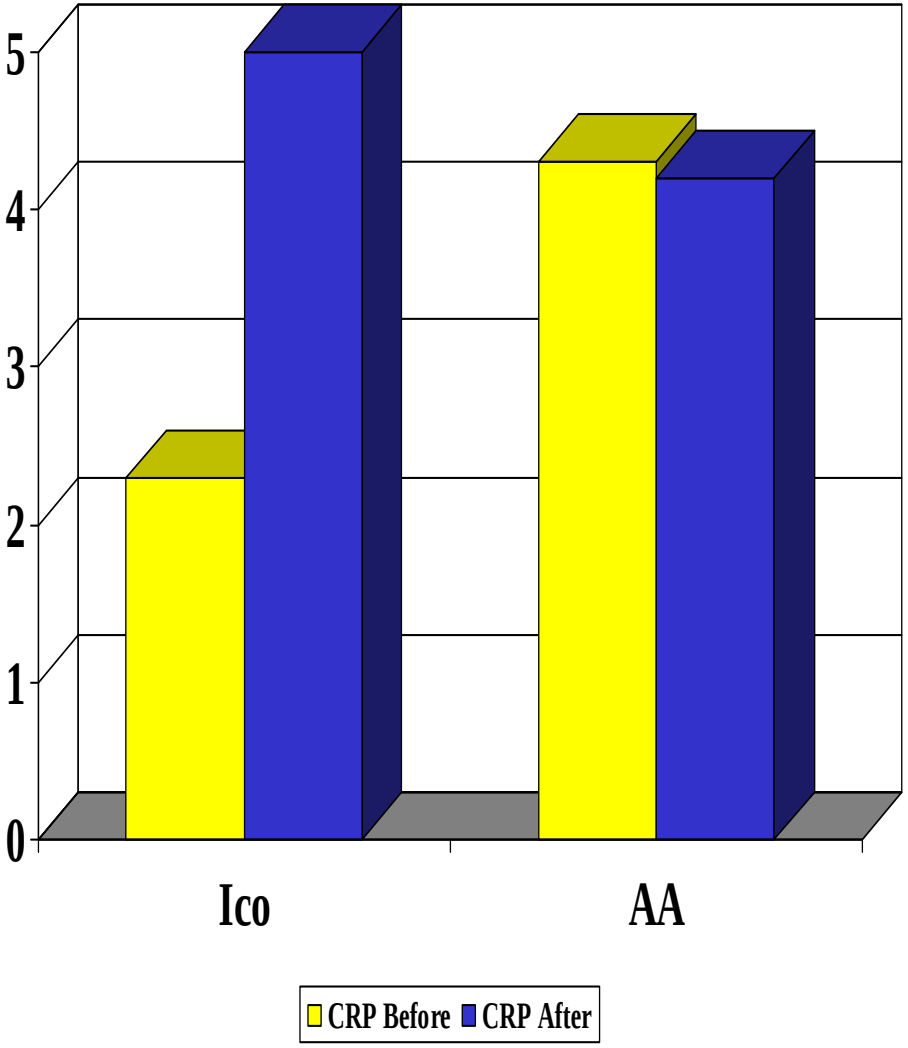
Gunal et al, AJKD, 37, 2001, 588-593

Icodextrin and fluid status

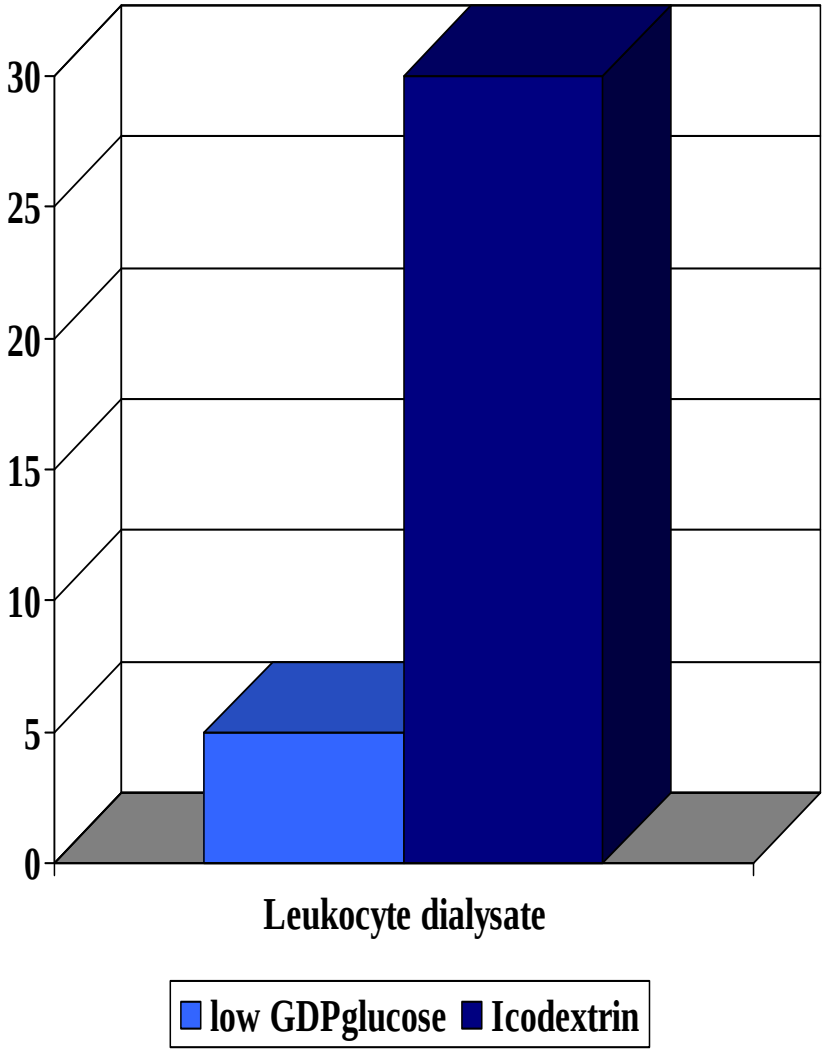


Konings et al; KI, 2003

Icodextrin and peritoneal inflammation



Martikainen et al, PDI 2005, 5



Parikova et al, Adv Perit Dial, 2003

Impact of education on diabetic compliance

- Intensive counselling of diabetic patients on PD
  - Importance of salt restriction
  - Importance of glucose monitoring
  - Deleterious effect of high glucose solutions

Quan and Wang T. et al, PDI 2006

Impact of education on diabetic compliance

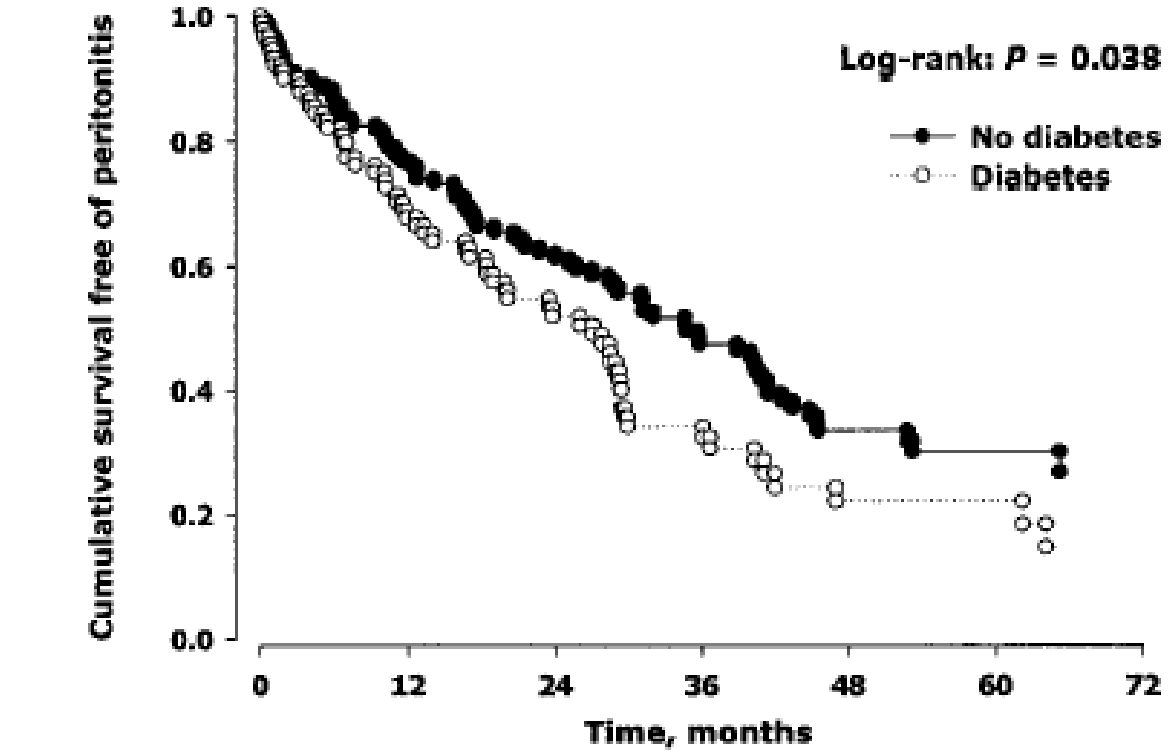
- **After 1 year:**
  - Compliance to salt restriction increased from 19.5 to 76.2%
  - Only 3/31 used 2.5% and 1/31 used 4.25%
  - Fluid status improved as measured by bio-impedance measurement

Quan and Wang T. et al, PDI 2006

Diabetes and peritonitis risk

Reference	Population	Infection free time (mths)	RR diabetics
Oo et al, AJKD 2004	USRDS	17.7 vs 15.8	1.13
Chow et al, PDI 2005	Hong Kong	82.3 vs 49.0	1.5
Lim et al, Nephrology 2005	ANZDATA	Not given	NS
Wang Q et al, AJKD 2003	Pensylvania	Not given (rate 0.65/year)	NS

Diabetes mellitus and PD peritonitis



Number at risk:				
No diabetes	155	70	24	5
Diabetes	89	36	10	1

Chow KM, PDI 2005;25:374-379

Peritonitis in diabetic PD patients

Cave diabetic rethinopathy and polyneuropathy: importance of the connectology and training

IP versus SC Insulin?

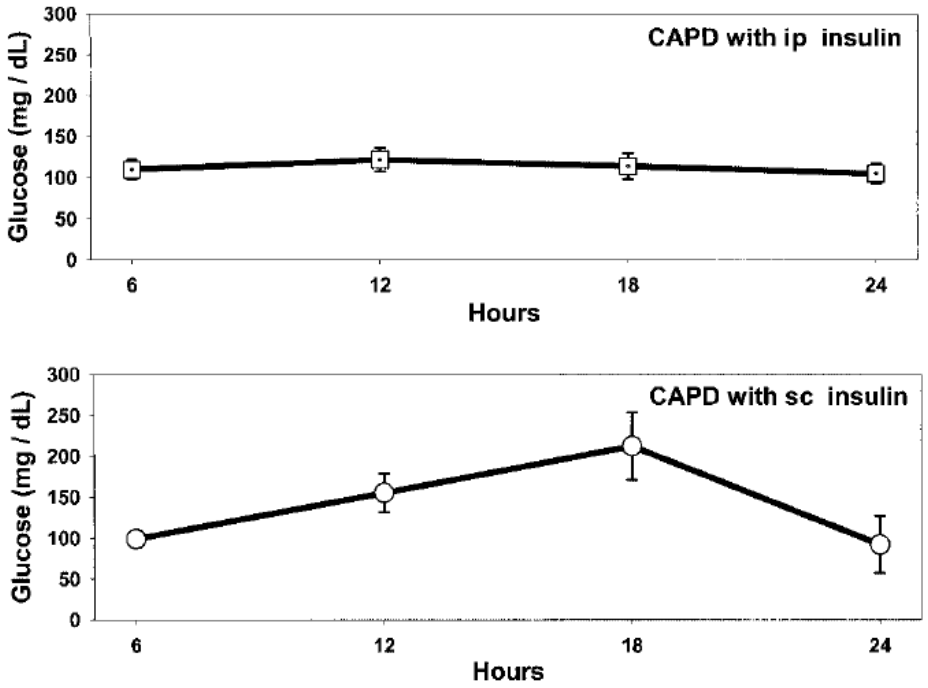
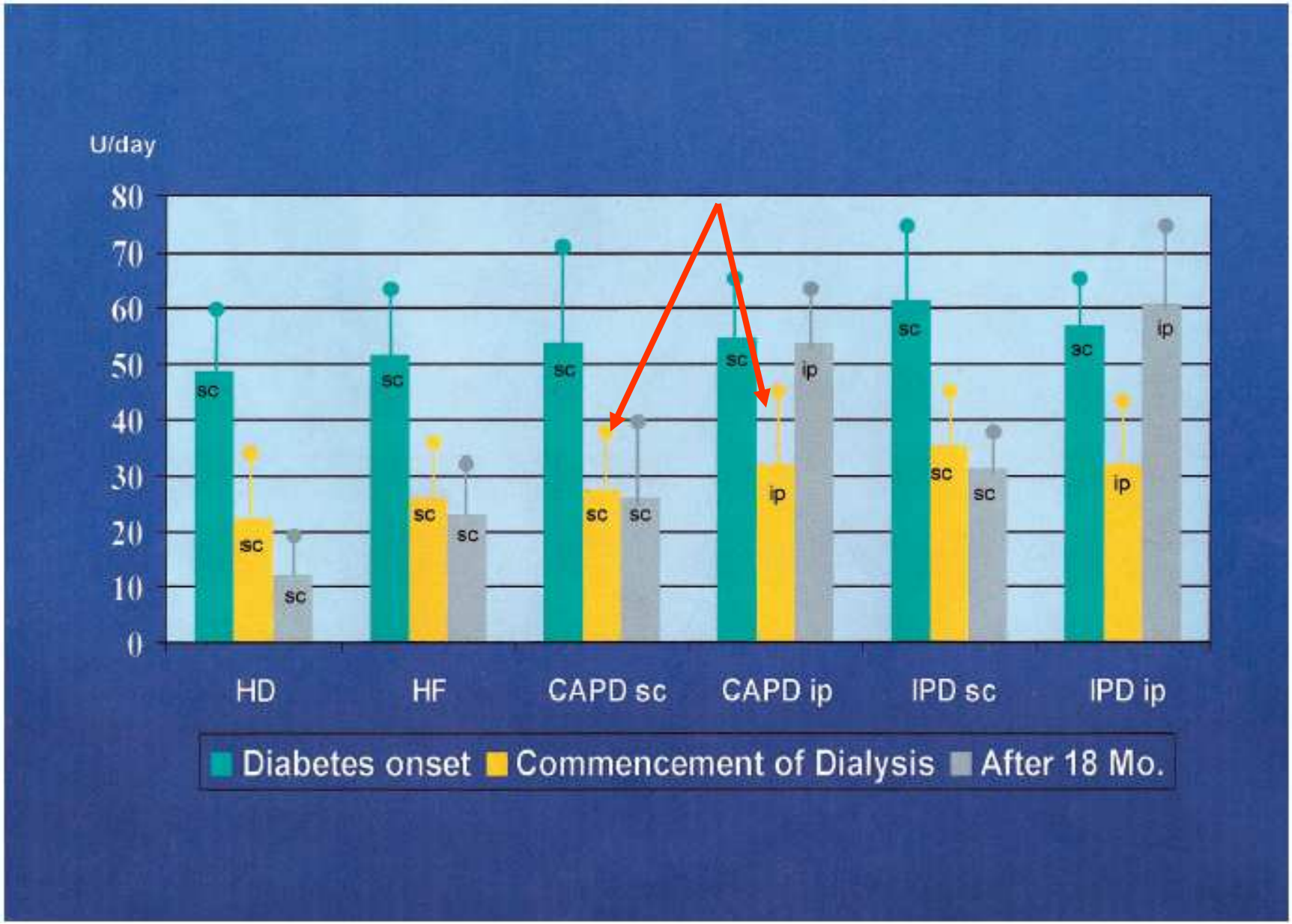


Figure 3. Diurnal blood glucose profile in continuous ambulatory peritoneal dialysis (CAPD) patients receiving either (A) intraperitoneally (ip) or (B) subcutaneously (sc) administered insulin.

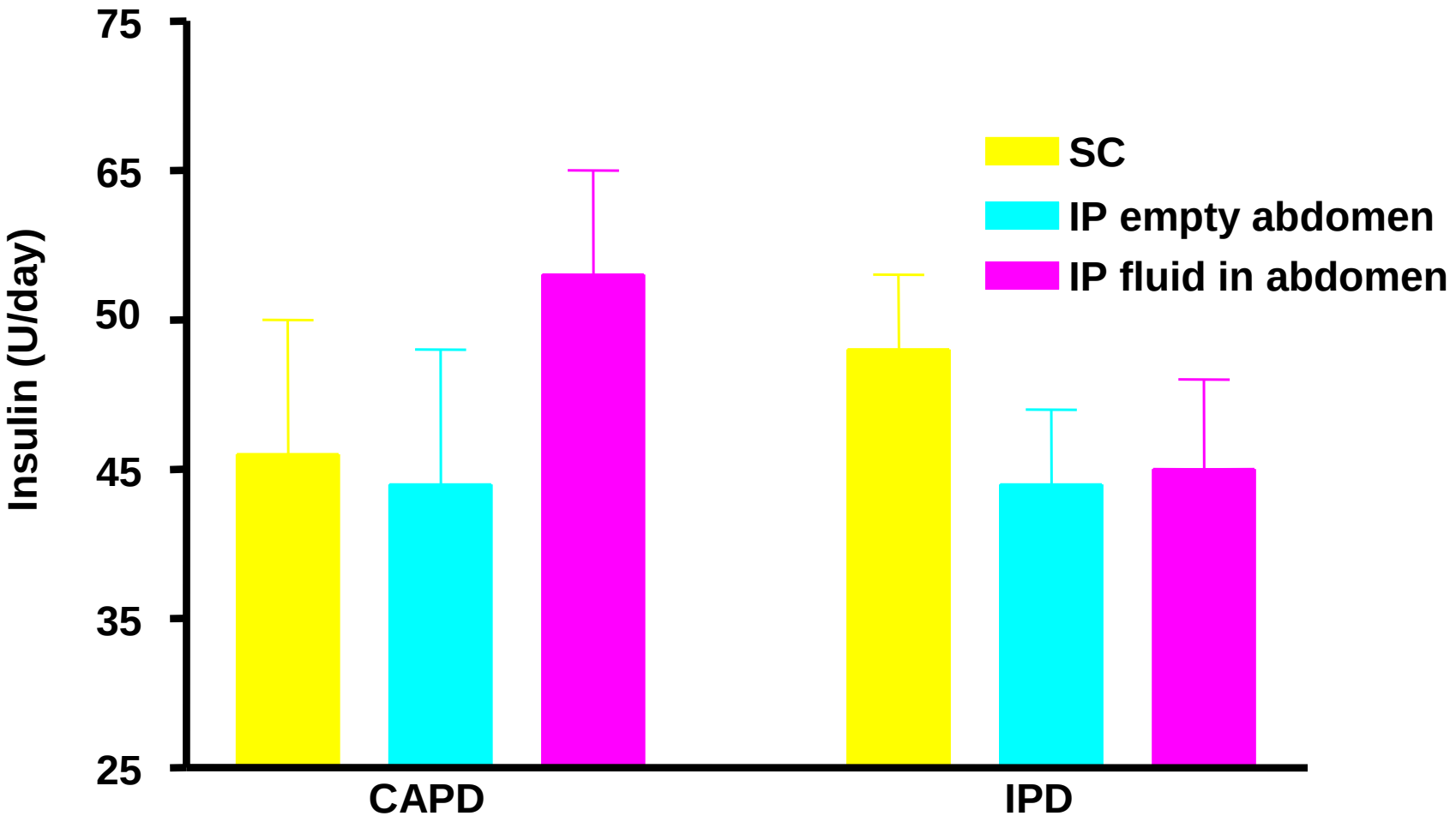
Quellhorst J Am Soc Nephrol 2002; 13:S92-S96

Insulin therapy in ESRD



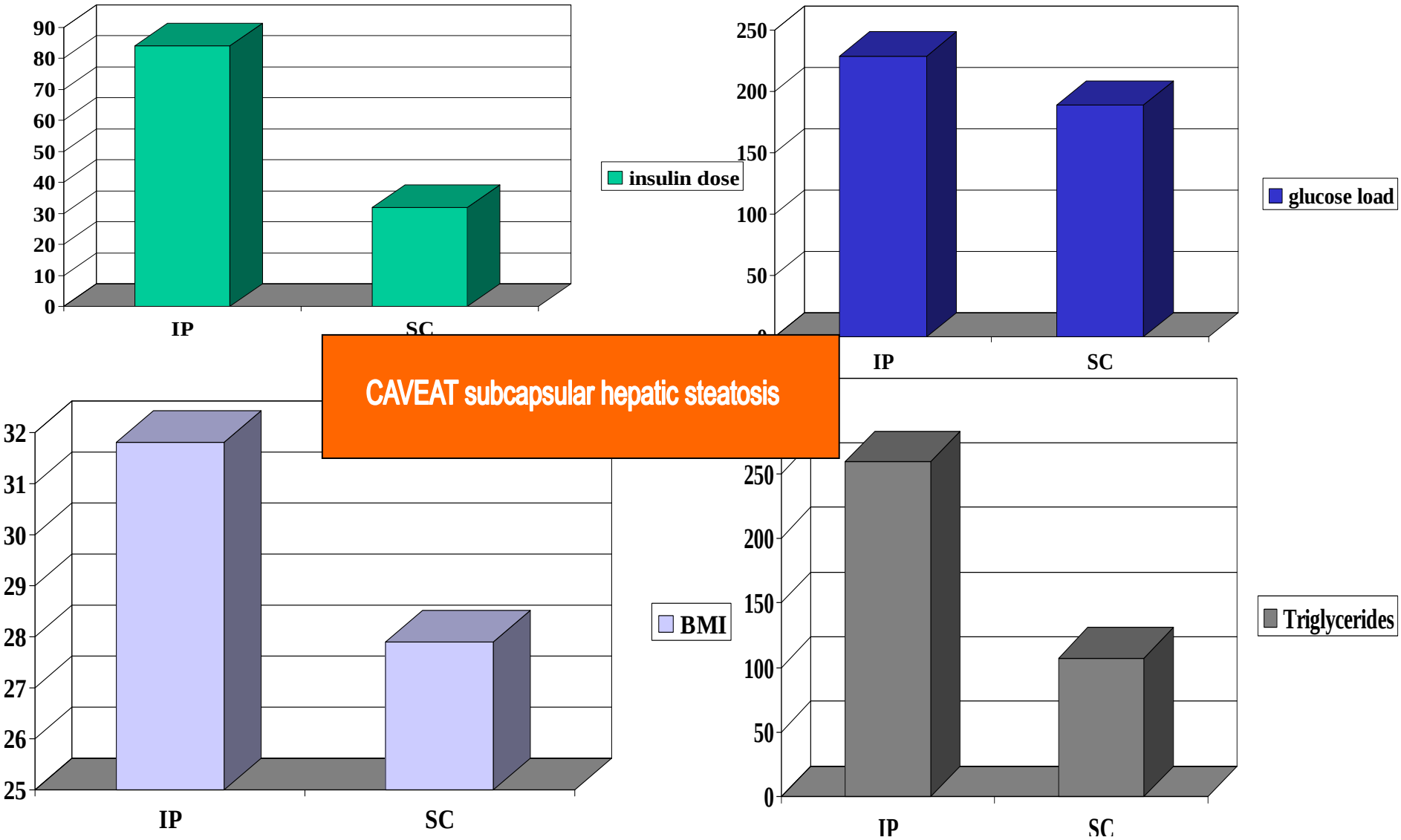
Ouellhorst et al. JASN 2002

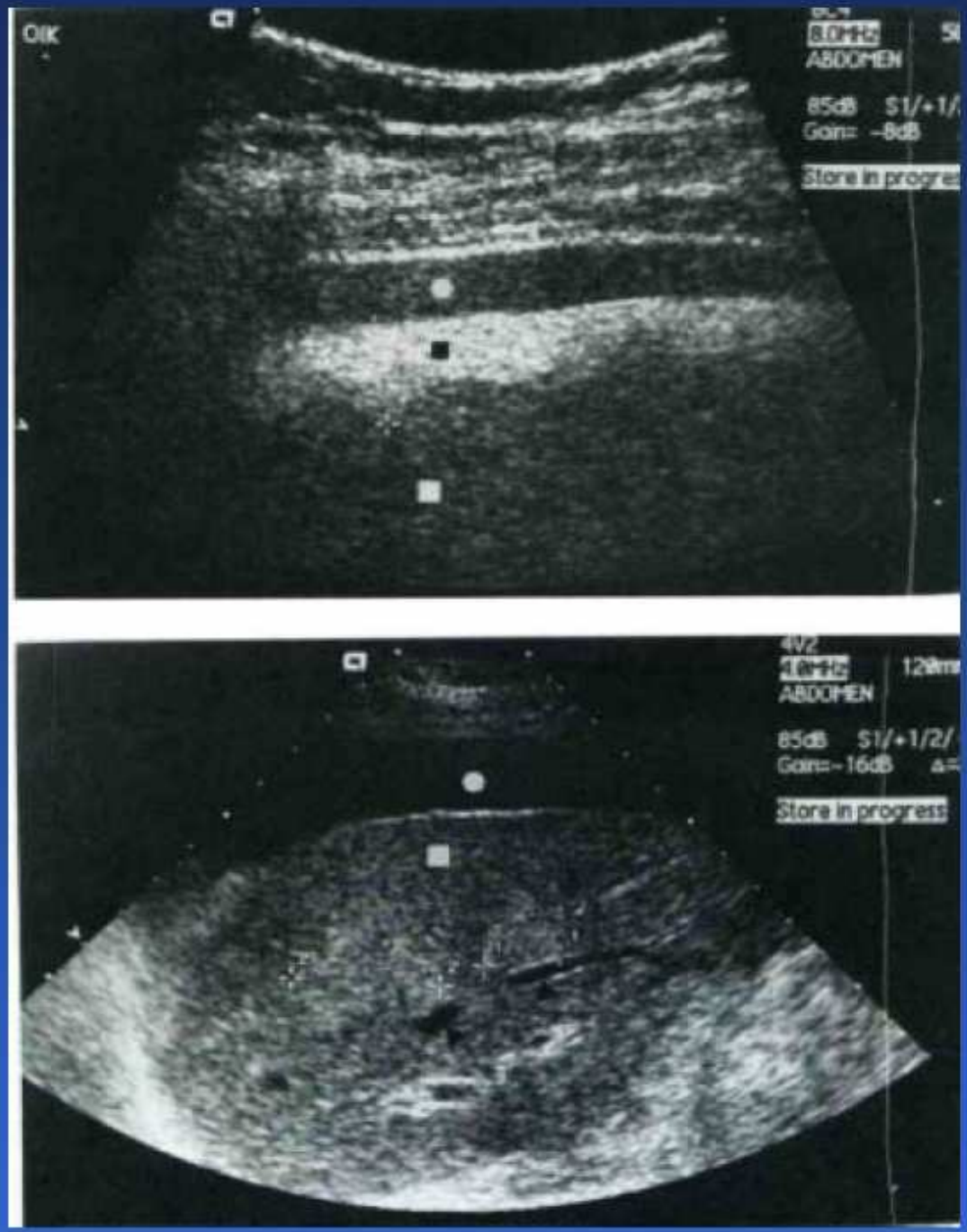
Daily insulin requirements for diabetic patients on peritoneal dialysis



Quellhorst J Am Soc Nephrol 2002; 13:S92-S96

Intraperitoneal vs Subcutaneous insulin (Torun et al, PDI 2005)





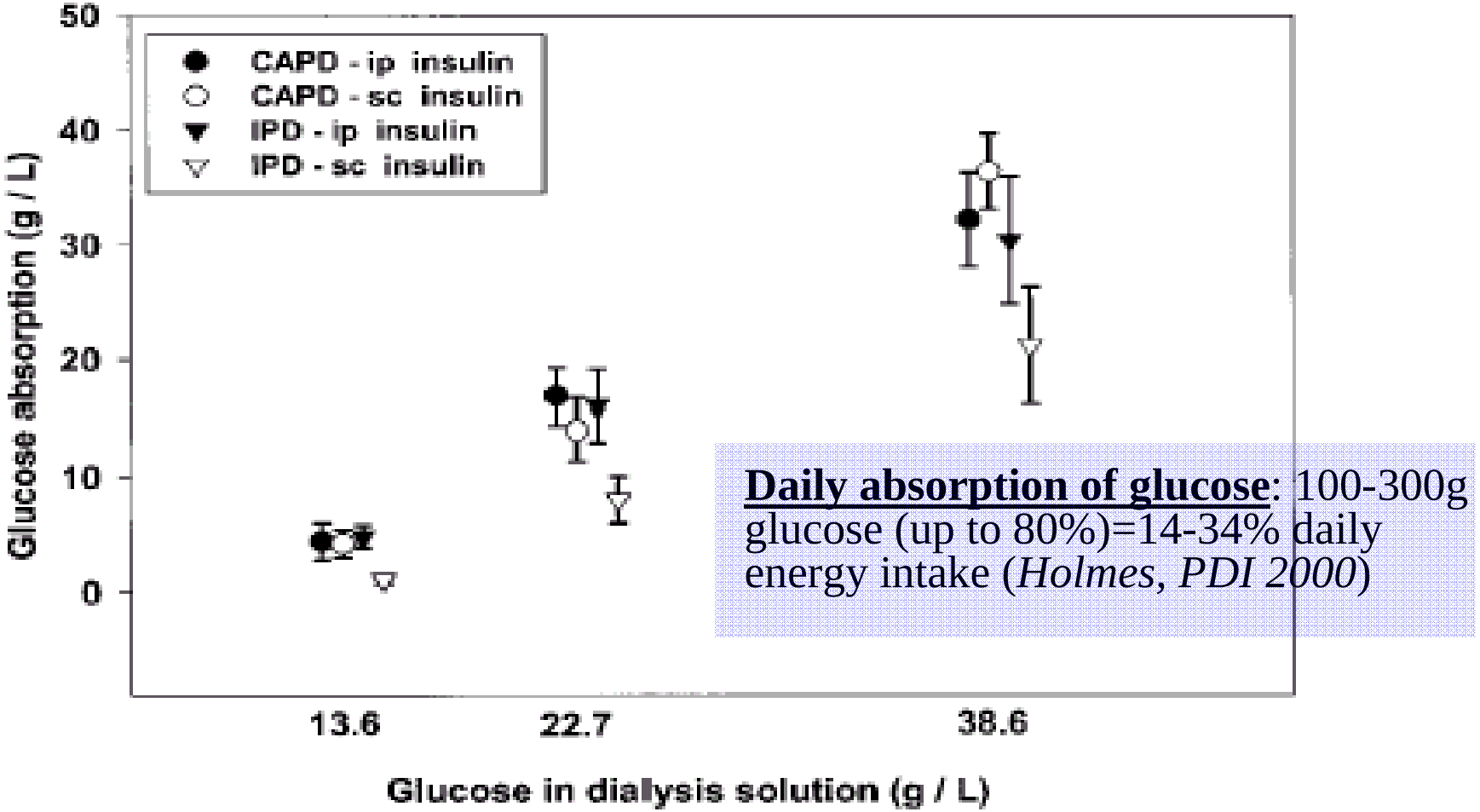
Hepatic subcapsular (upper) and intrahepatic steatosis (lower) after ip insulin

sc n=8, 0/8

ip n=8, 7/8

PDI 20 (6): 637-642, 2000.

Glucose absorption from the abdominal cavity with different glucose dialysates according to insulin administration

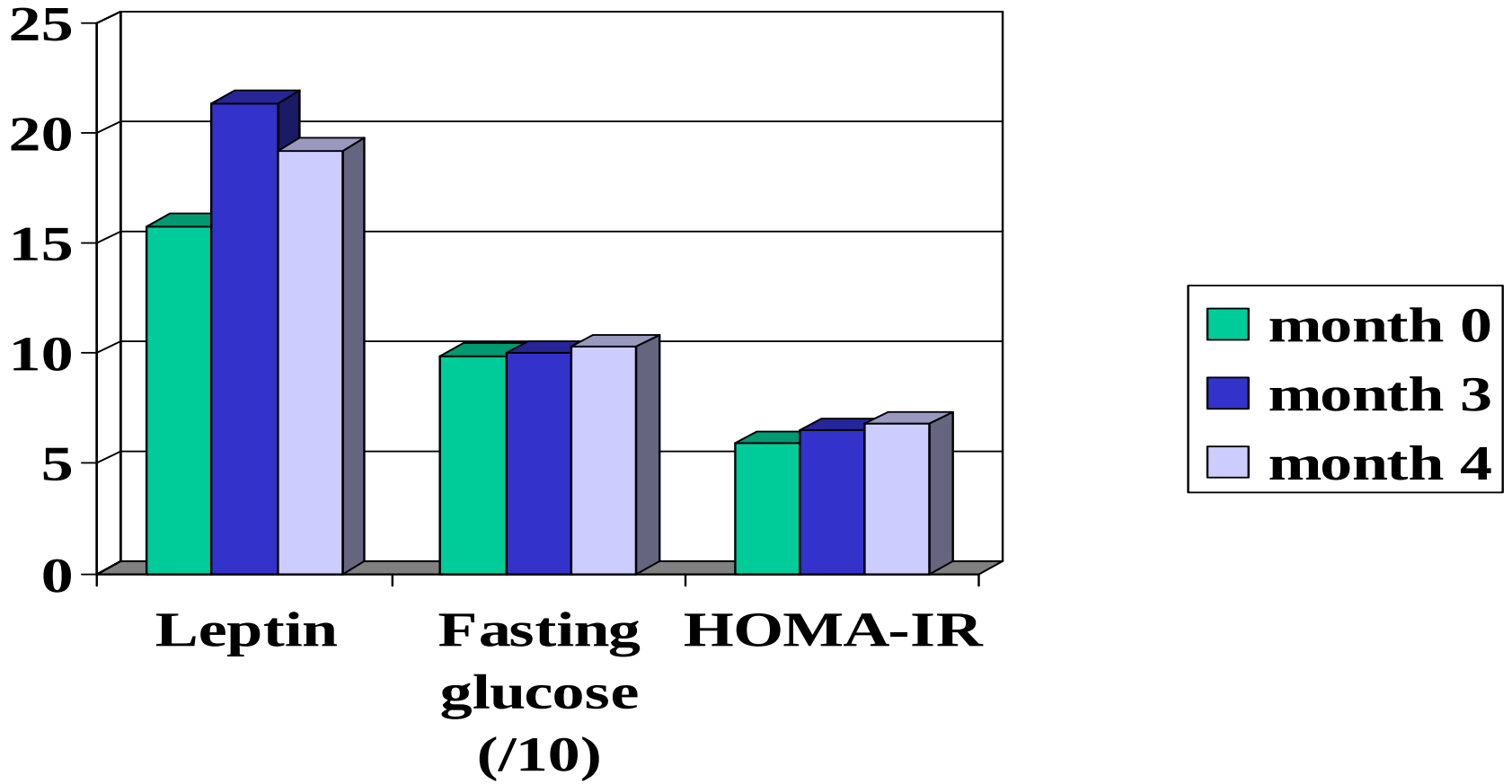


Daily absorption of glucose: 100-300g glucose (up to 80%)=14-34% daily energy intake (*Holmes, PDI 2000*)

Quellhorst J Am Soc Nephrol 2002; 13:S92-S96

Do glucose free solutions lead to better glycemia control?

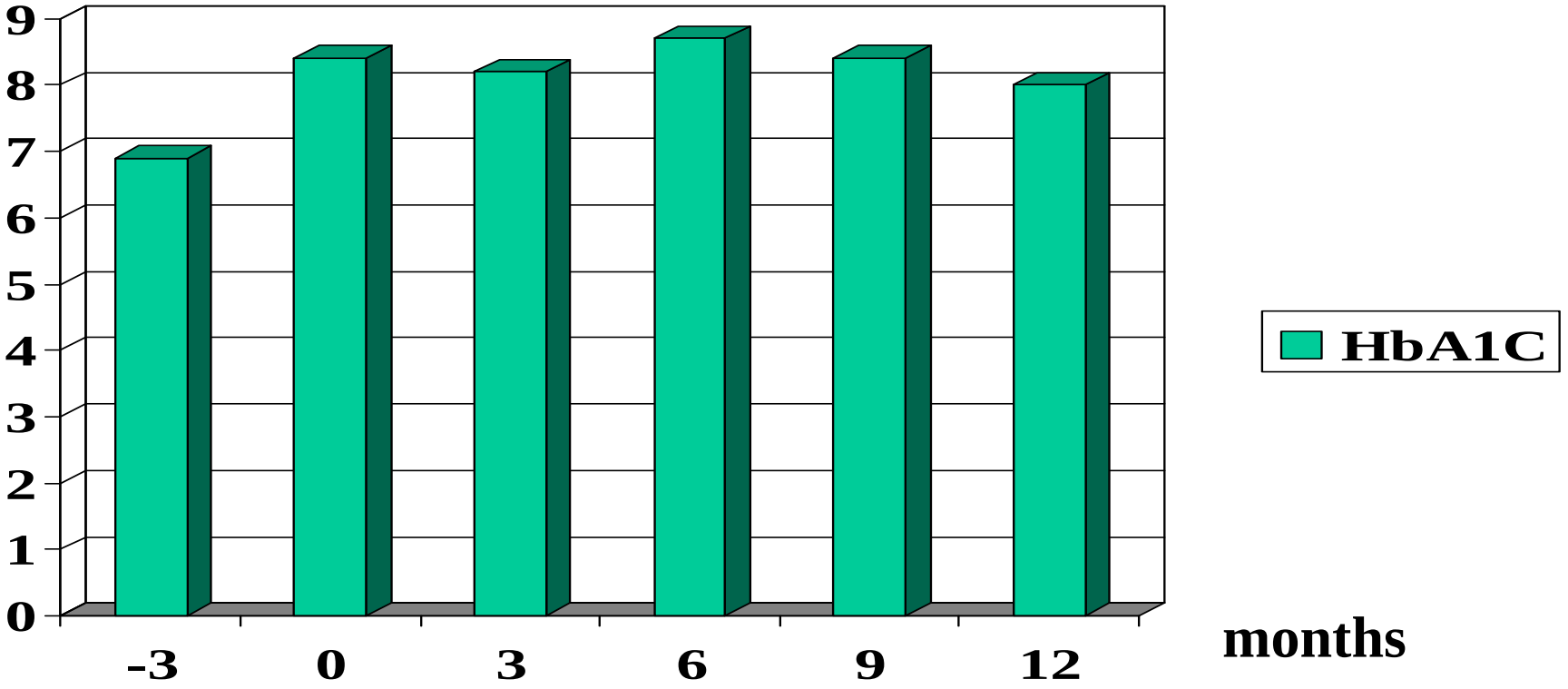
Switch to amino acid 1*



Yang et al, NDT 2005

Do glucose free solutions lead to better glycemia control?

Switch to icodextrin

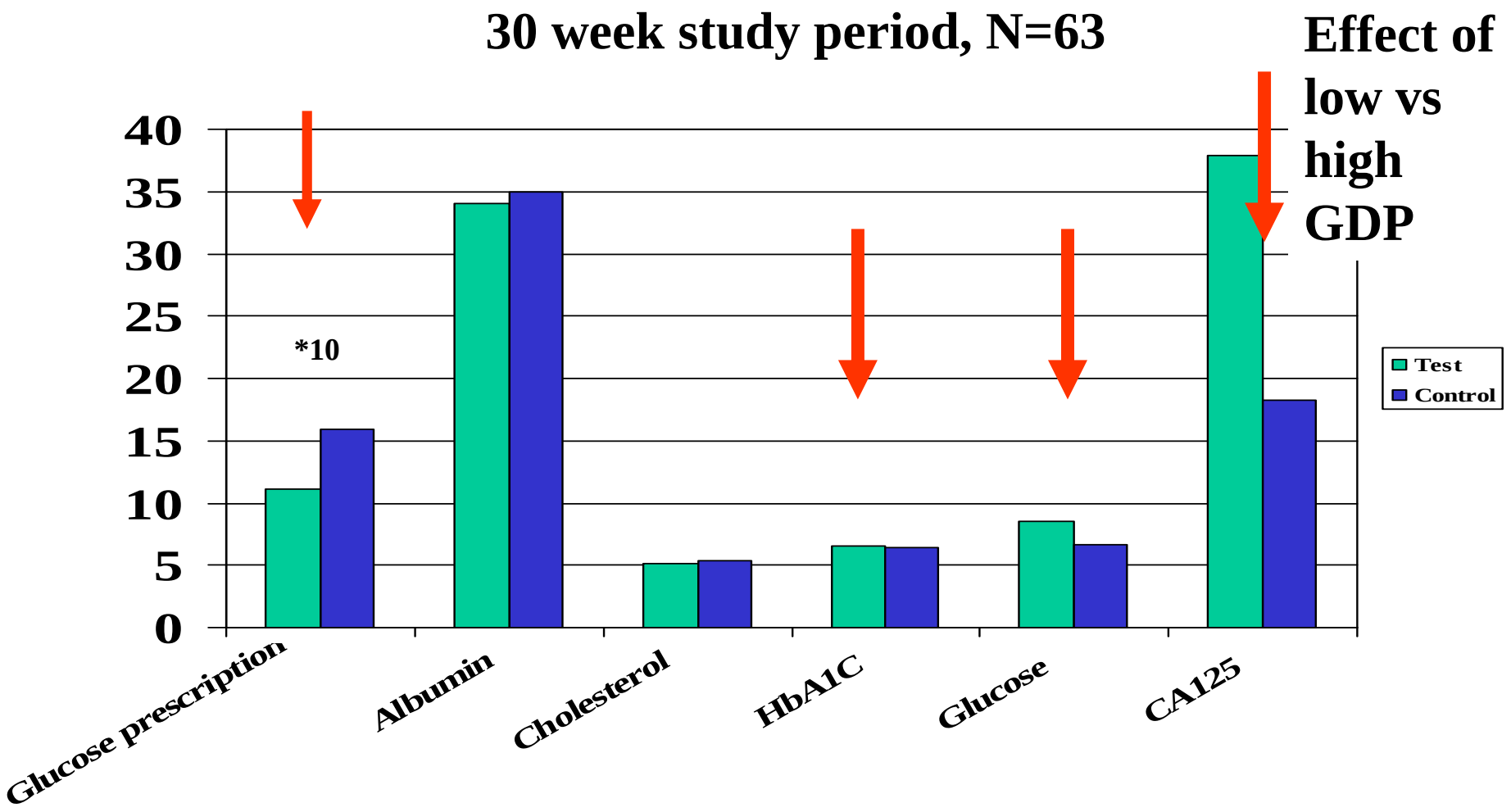


Oreopoulos et al, PDI, 2004

Do glucose free solutions lead to better glycemia control?

Ico+AA+2Ph vs 4*conventional glucose

30 week study period, N=63

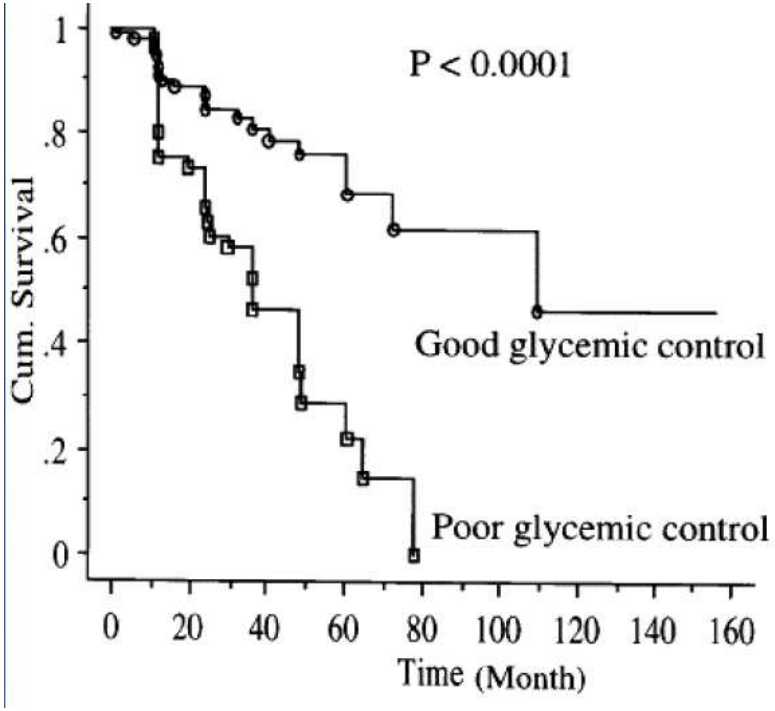


Ter Wee et al, PDI, 2005, S3, S64

Is excellent glycemic control efficacious in the prevention of later complications?

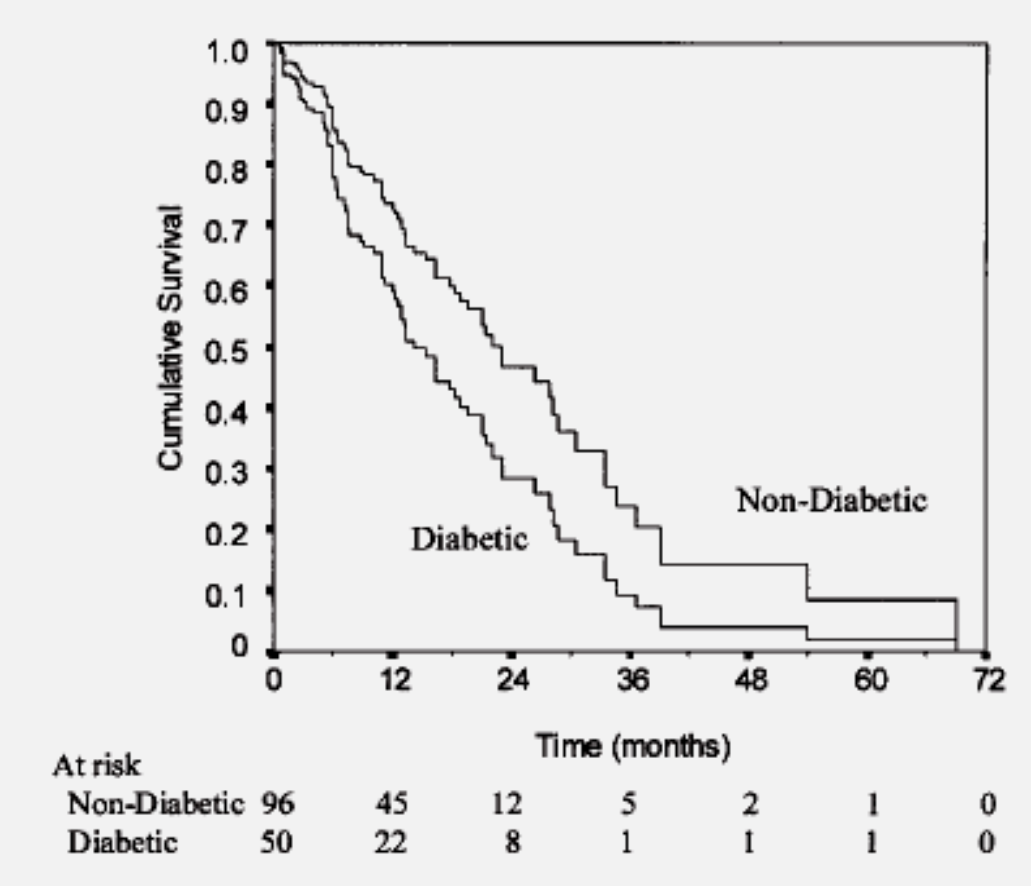

Very efficacious!!

Poor pre-ESRD glycemic control leads to poor outcome after dialysis



Wu M, NDT 1997;12:2105-2110

Diabetes and peritoneal dialysis: What about RRF?



Johnson, PDI 2003;23:276-83

Interventions that delay progression of CRF: ACE Inhibitors

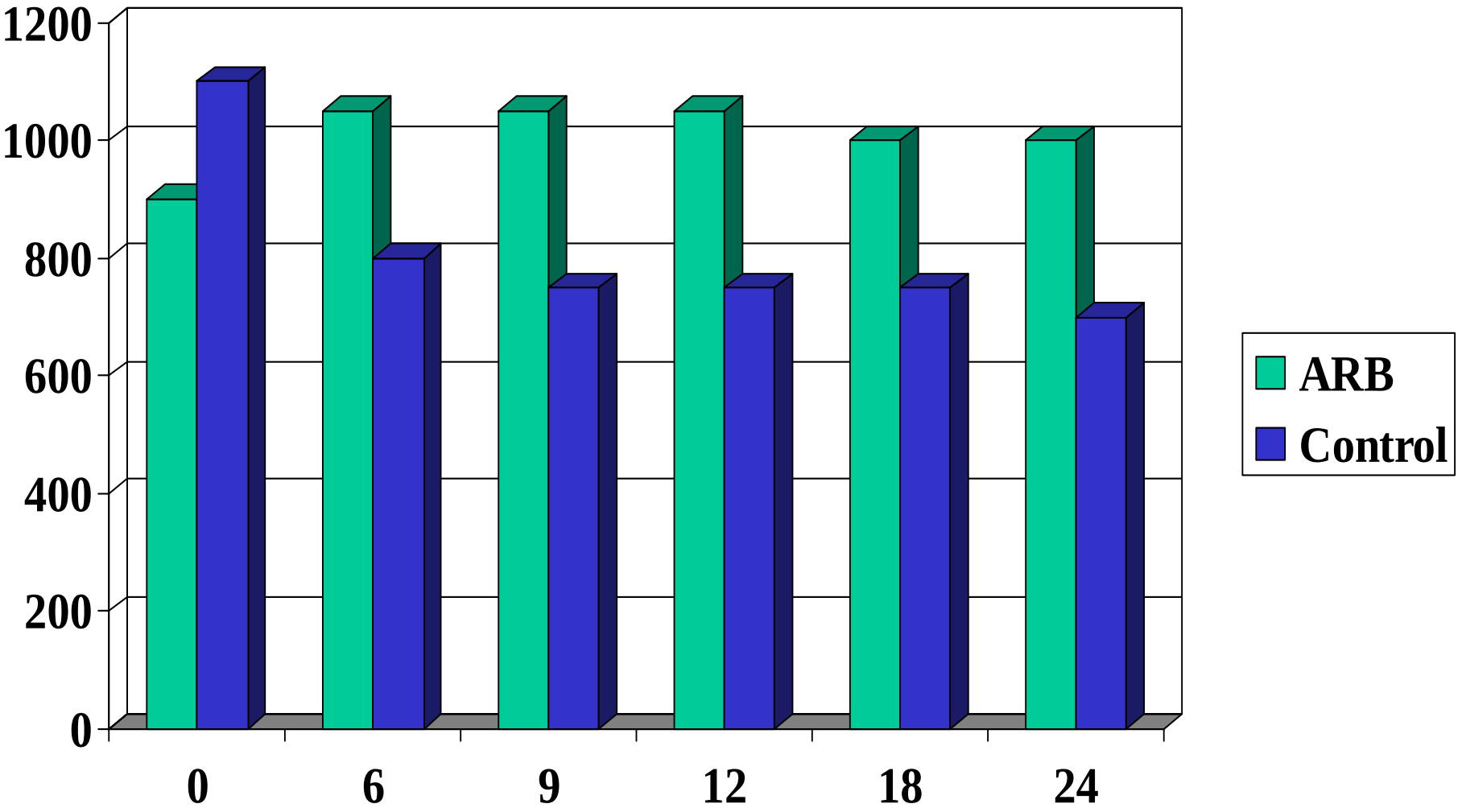
- A meta-analysis[1] of 10 randomized trials found:
  - Slower decline in RRF as opposed to other antihypertensives or placebo.
  - ACE inhibitors were associated with a statistically significant reduction in risk of ESRD, but not of death.
- In ESRD patients: role of ACE-I less clear:
  - Moist[2] et al: ACE-I protect
  - Shingal[3] et al: Trend, but not significant

[1] Giatras I, et al, *Ann Intern Med*, 1997; 127:337-45
[2]Moist et al, JASN 2000, 11, 556-564

[3] Shingal et al, PDI, 20, 429-438

ARB's and PD and RRF

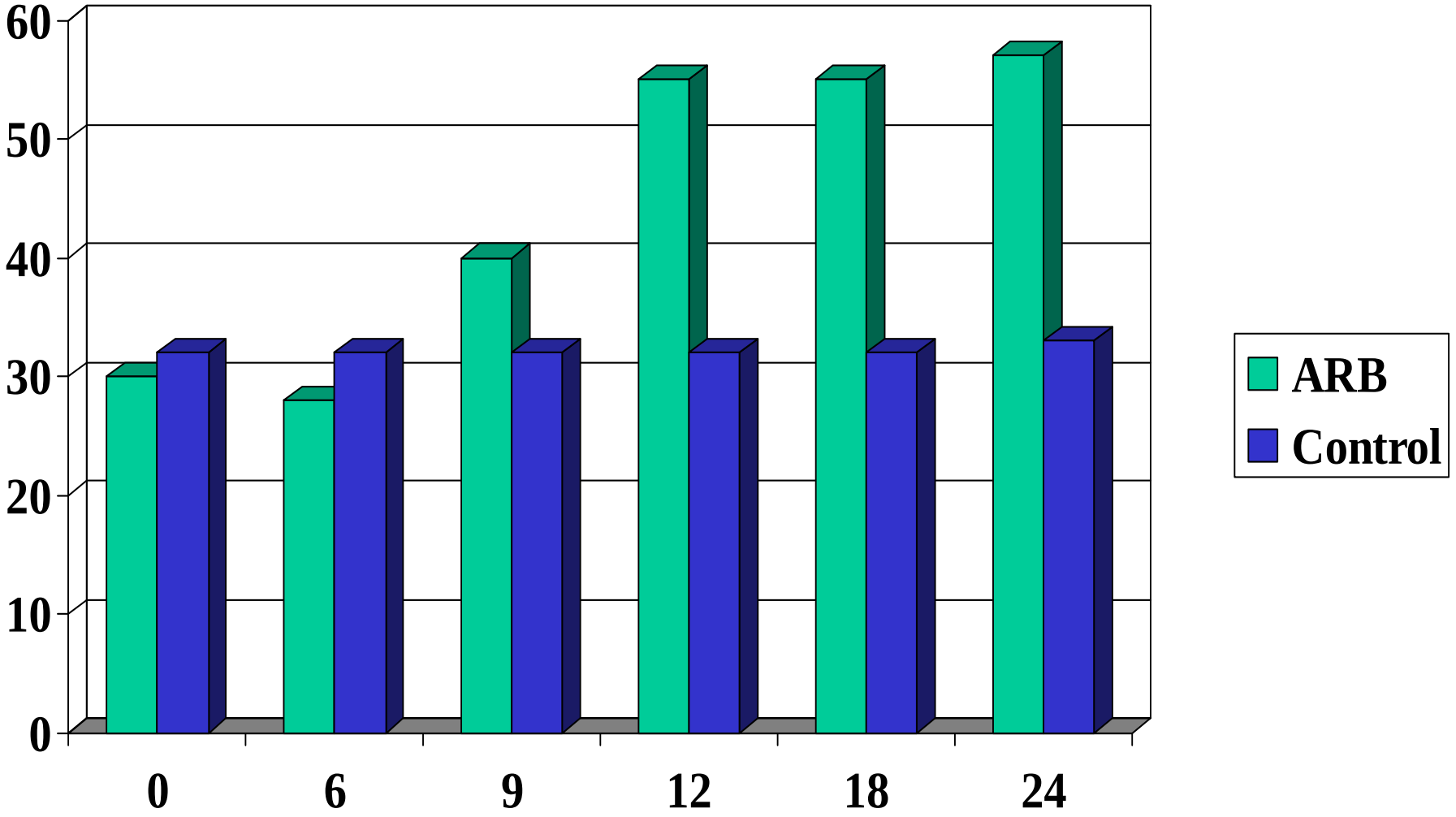
Urine in ml/24 hr



Suzuki et al, AJKD, 43,1056

ARB's and PD and RRF

Peritoneal Ccrea (l/week)



Suzuki et al, AJKD, 43,1056

Conclusion

- **No doubt that diabetes is an evil disease, with negative impact on outcome of ESRD patients**
- **PD in an integrated care approach is a suitable alternative for diabetics IF**

  - **Attention to salt and fluid restriction and preservation of RRF**
  - **Attention to glucose regulation**
  - **Attention to obesity**
  - **Use of ACE-I or ARAB**
  - **Low –GDP mandatory!**
  - **Icodextrin: only if all other measures fail**

Not to forget..

Lesson of the week

Spurious hyperglycaemia and icodextrin in peritoneal dialysis fluid

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Metabolites of new peritoneal dialysis fluids may cause spurious hyperglycaemia and inappropriate insulin treatment

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Diabetes mellitus, in particular type 2, has become more common, and the trend is likely to continue.[1] Associated comorbidity is also more common—for example, diabetes is now the most common cause of dialysis dependent renal failure in the Western world.[2] In the United Kingdom between 1991 and 1998, the incidence of new patients on dialysis increased from 67 to more than 90 patients per million population, and the prevalence of diabetes in people receiving dialysis has increased from 16% to 19%.[3]

The increasing demand for dialysis and slower growth in capacity for haemodialysis has reinforced the need for an integrated approach to providing dialysis. Peritoneal dialysis is the preferred option for a proportion of patients with end stage renal failure.[4] A subgroup of patients has difficulties with removing fluid. This can be improved with an alternative osmotic agent based on a polymer of glucose—icodextrin.[5] We report a severe potentially clinical consequence of using icodextrin in a diabetic patient, which although mentioned in a specialist journal is still not widely recognised. This issue is even more important given the increasing number of diabetic patients with end stage renal failure. About 500 patients in the United Kingdom use icodextrin daily.

In the emergency department the man seemed comfortable at rest but was feverish with a temperature of 37.2°C. His pulse was 85 beats/min and blood pressure 160/80 mm Hg. Oxygen saturation was 94% on air. He had a raised jugular venous pressure and heard crackles at the base of both lungs. A chest x ray showed interstitial shadowing but no focal consolidation. The finger stick glucose reading was 17 mmol/l.

The team diagnosed him as having chest infection and transferred him to a sister hospital. During transfer the patient's consciousness decreased: he became sweaty and developed slurred speech. On arrival at the new hospital, the patient had a grand mal seizure. Finger stick glucose testing gave a reading of 15.4 mmol/l. He was given 5 mg diazepam and the fit subsided. Soon after, laboratory blood tests found that venous glucose concentration was only 1.2 mmol/l. On treatment with intravenous glucose the patient recovered.

The admitting doctors started antibiotics and insulin using a sliding scale. Two hours later, the patient had another grand mal seizure and they gave further bolus of diazepam. The glucose finger stick reading had increased again, to 14 mmol/l, but venous glucose concentration was 1.5 mmol/l. They gave further intravenous glucose and the patient recovered. A sample of blood on test sticks from two different machines gave

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