

Université Claude Bernard Lyon 1



Epidemiology, Diagnostic and treatment for Protein Energy Wasting in Dialysis

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ESRD

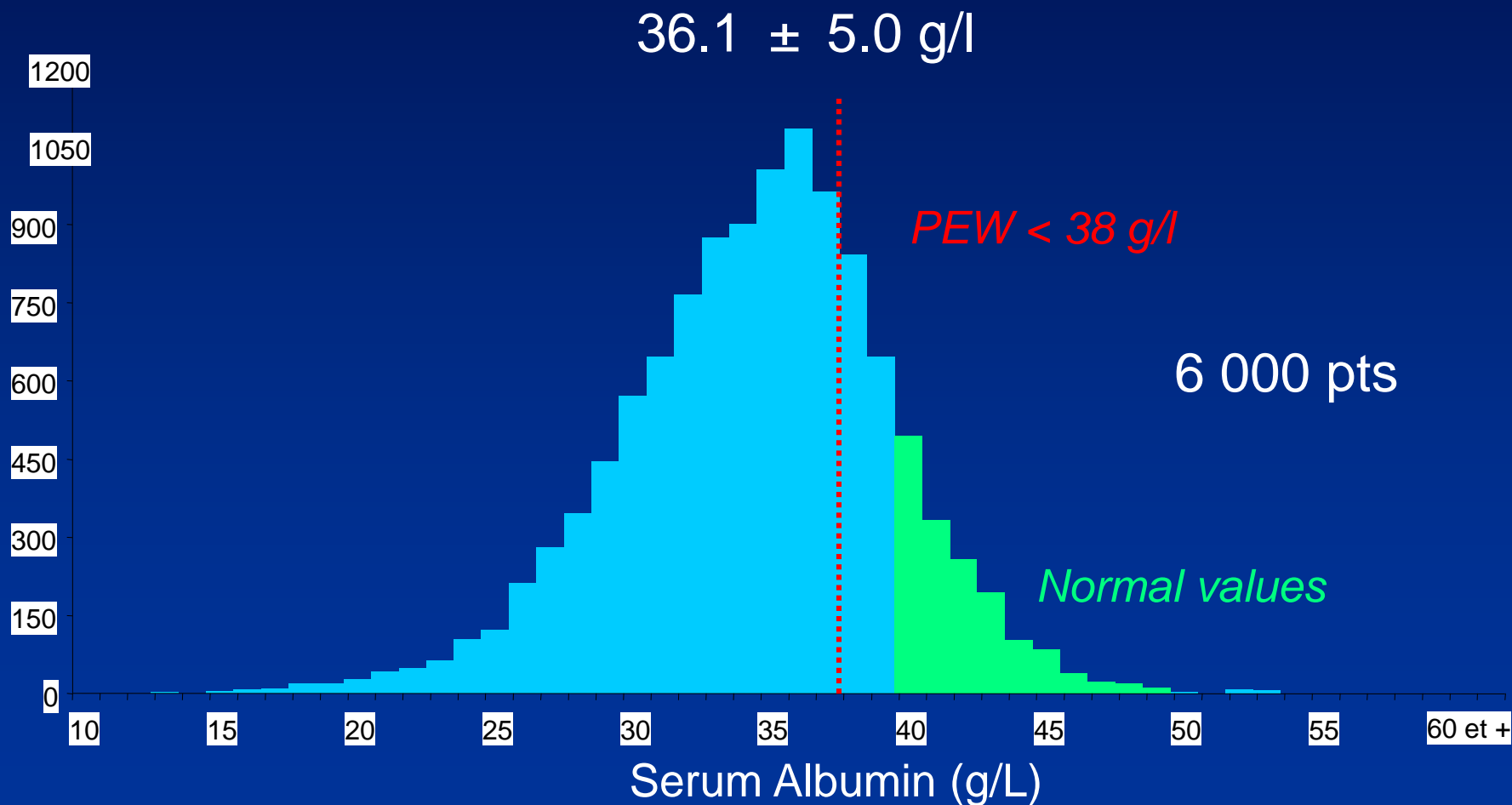
Definition of Malnutrition status

and

How to predict survival

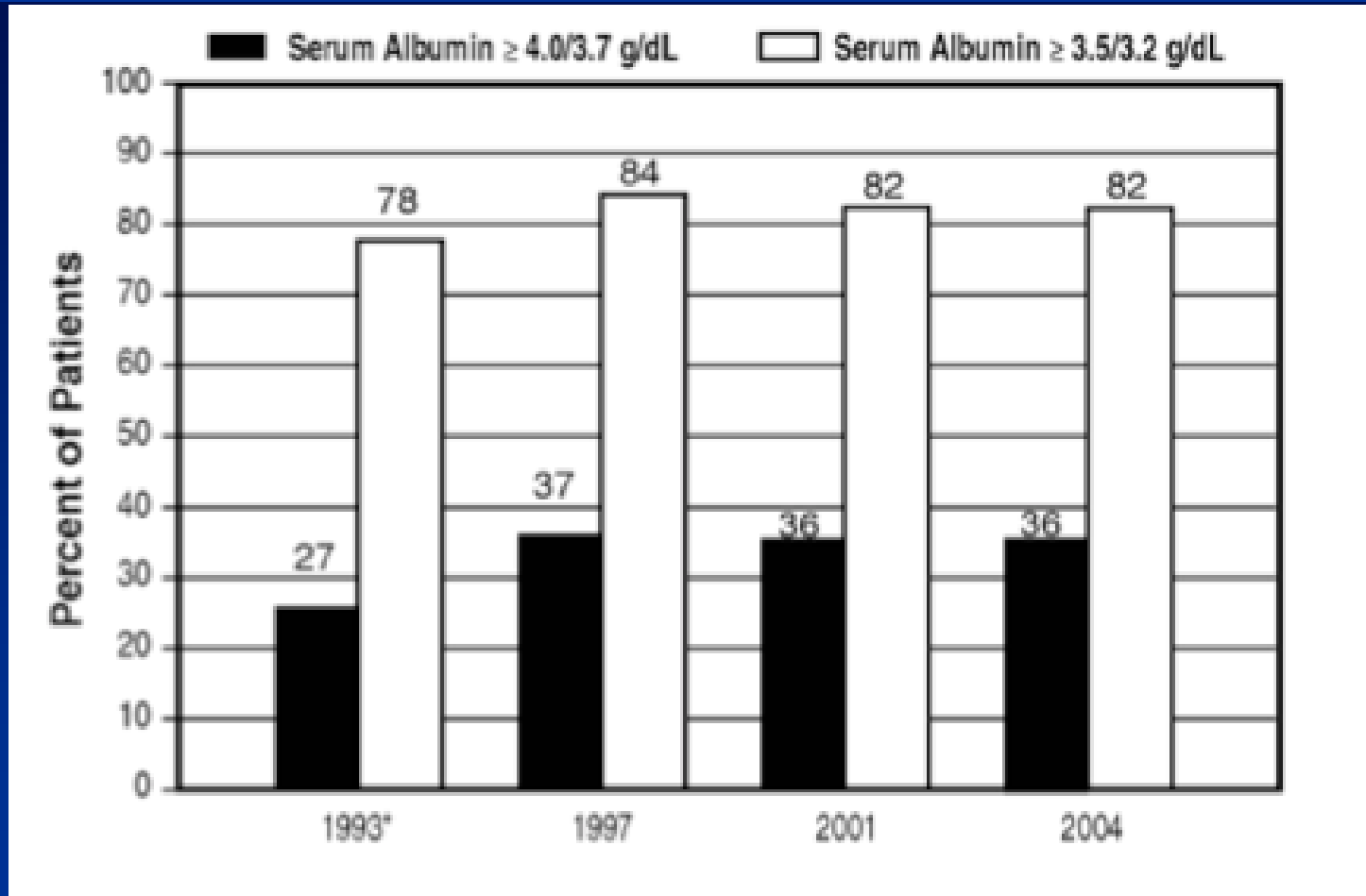
Low serum albumin in French dialysis Pts

Observatoire Phosphocalcique, January 2011



Serum Albumin of MHD patients, USA, 1993-2004

ESRD Clinical Performance Measures Project



Protein Energy Wasting - 2008

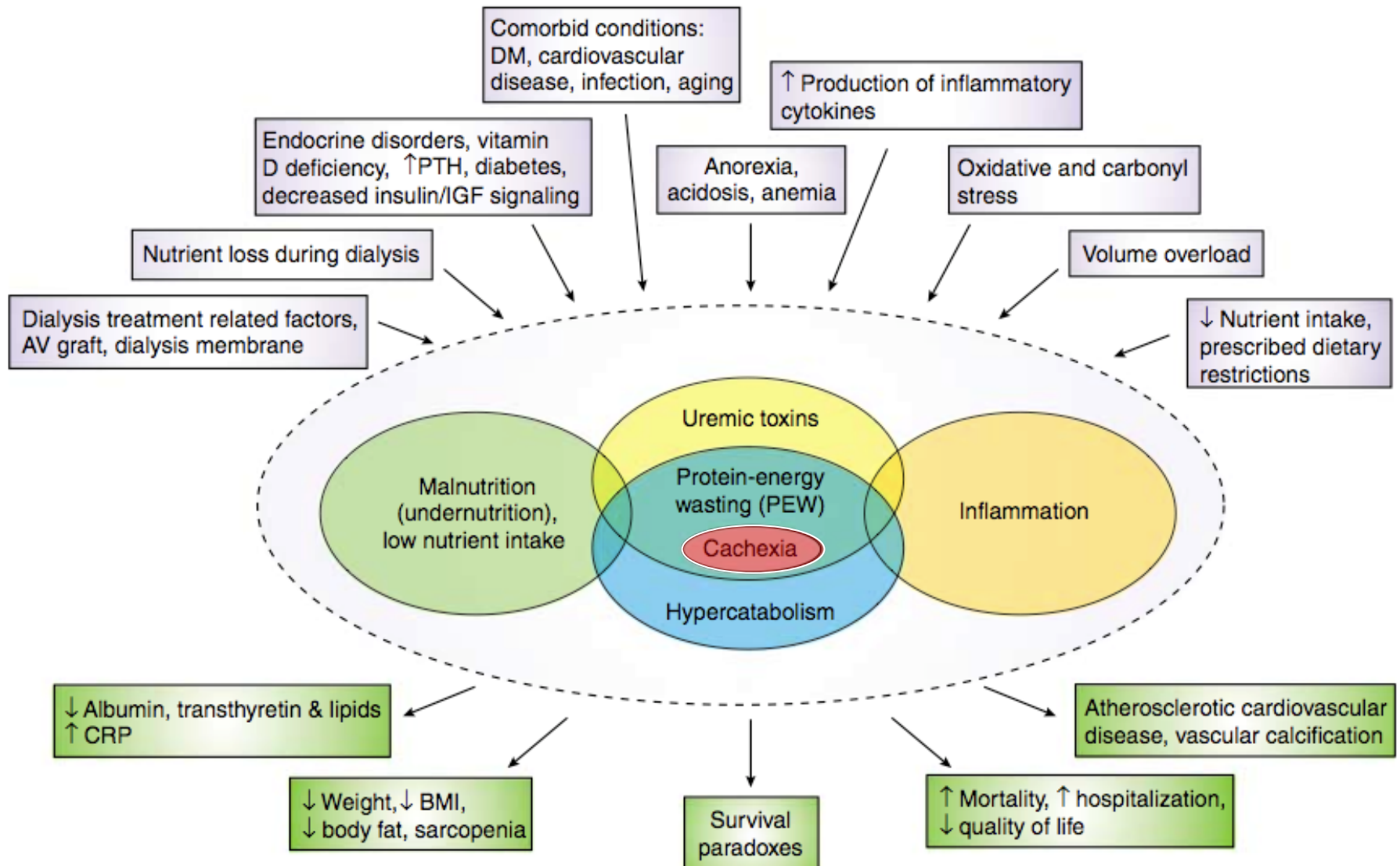
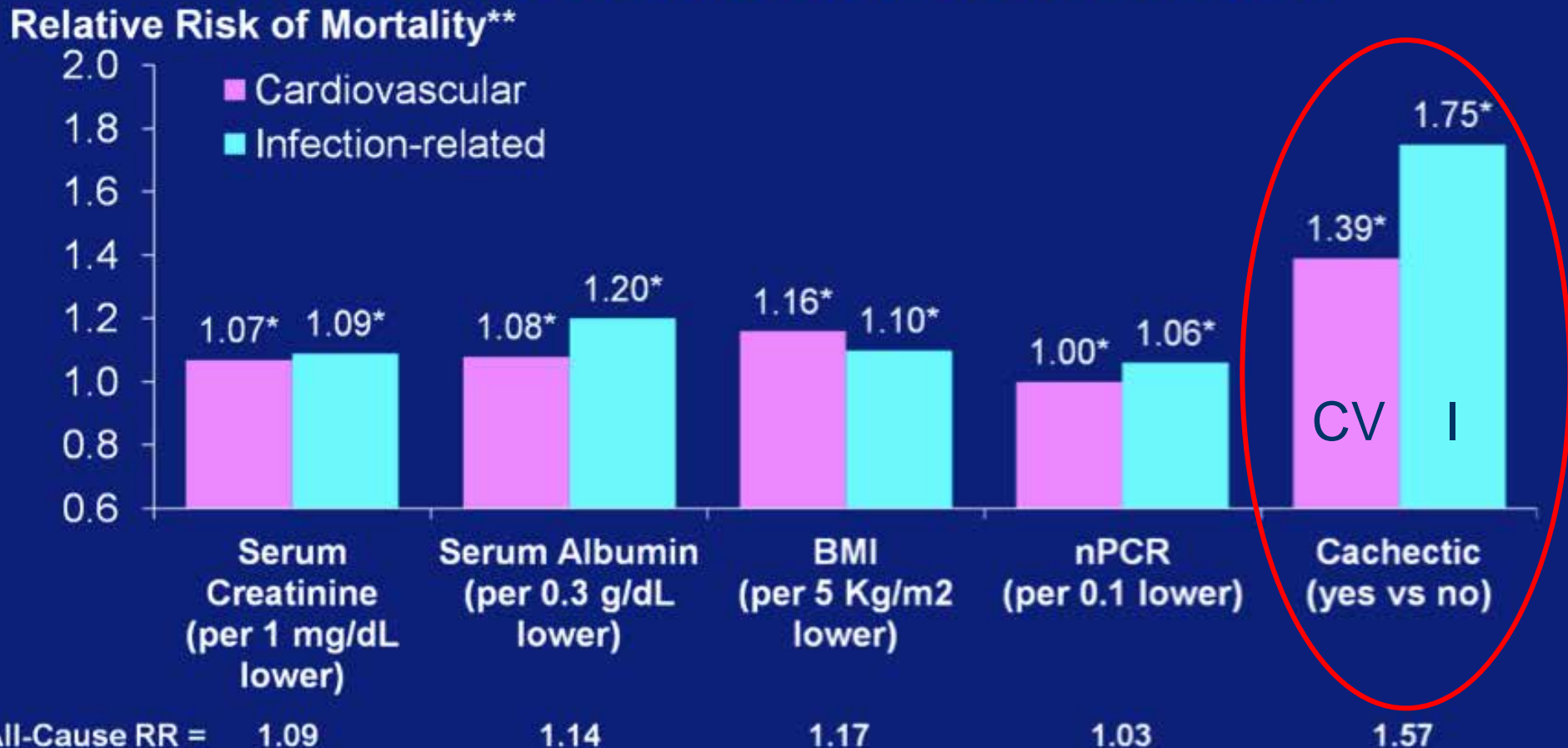


Figure 1: Adjusted RR of death due to cardiovascular and infection-related causes associated with nutritional indicators



* $p < 0.01$;

** Relative risks were adjusted for age, sex, race, vintage, 14 summary comorbidities, neutrophil/lymphocyte ratio and dialysis by catheter; BMI = body mass index; nPCR = protein catabolic rate; RR = relative risk



Protein Energy Wasting - 2008

Gr 1: Biology

Gr 2: Body Mass

Gr 3: Muscle

Gr 4: Dietary intake

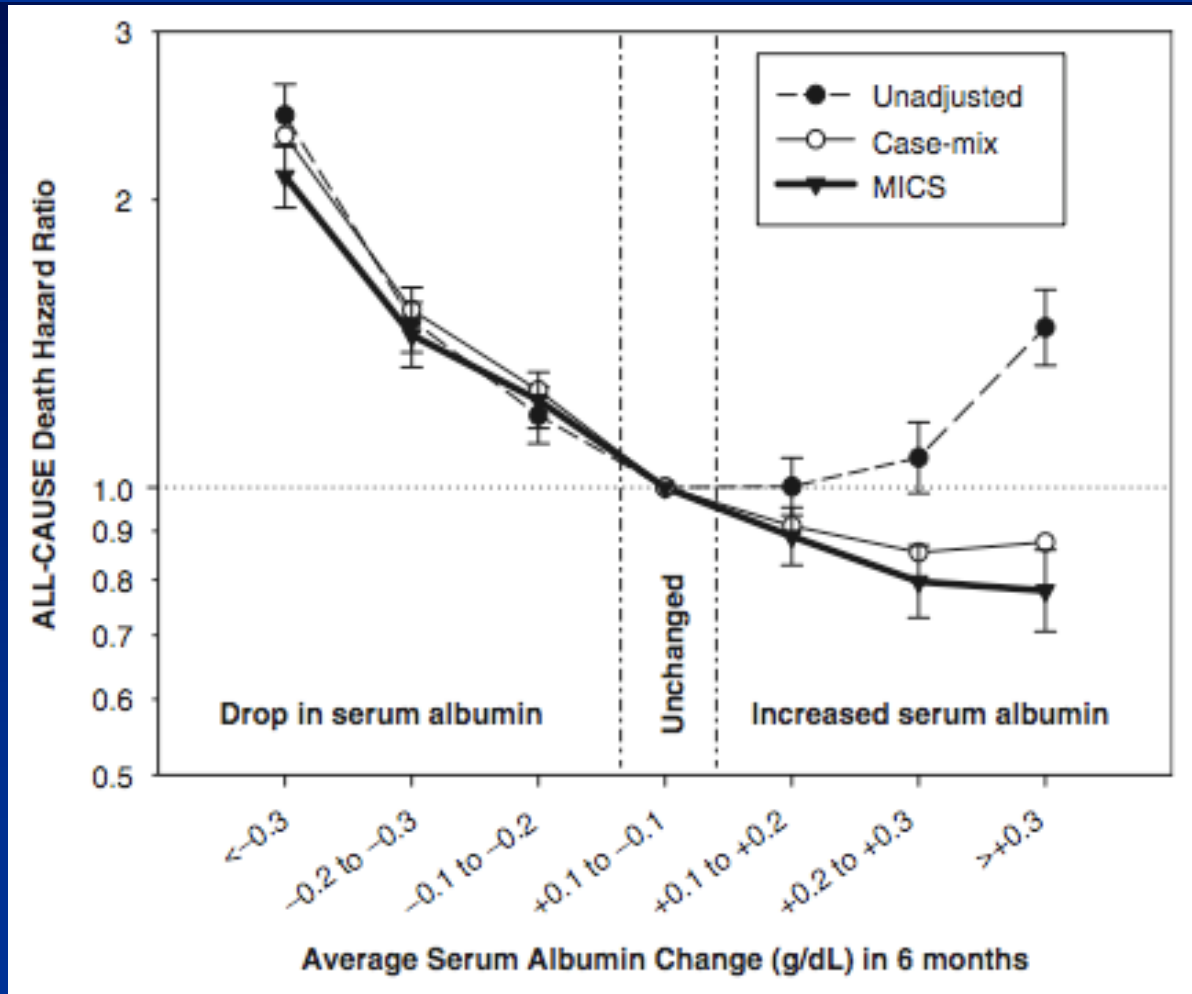
At least one criterion in 3 of the 4 groups

Protein Energy Wasting - 2008

Biology

- Serum Albumin < 38 g/l (BCG)
- Gr 1 - Serum prealbumin < 300 mg/l
- Serum cholesterol < 1 g/l

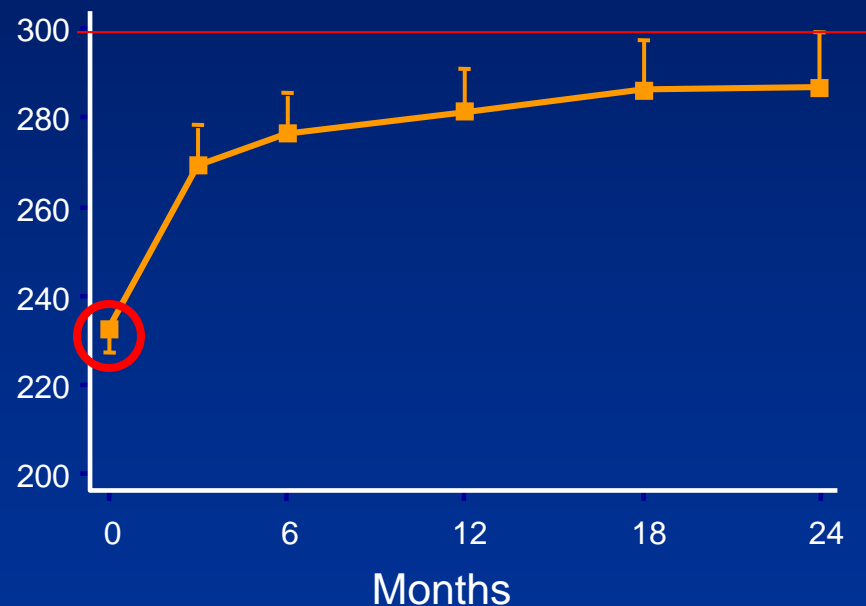
Short term albumin change predicts long-term survival



Serum Prealbumin response to renutrition

FineS study, oral \pm IDPN support in malnourished MHD pts

Serum prealbumin
mg/L



+ 55 mg/l
+ 23%

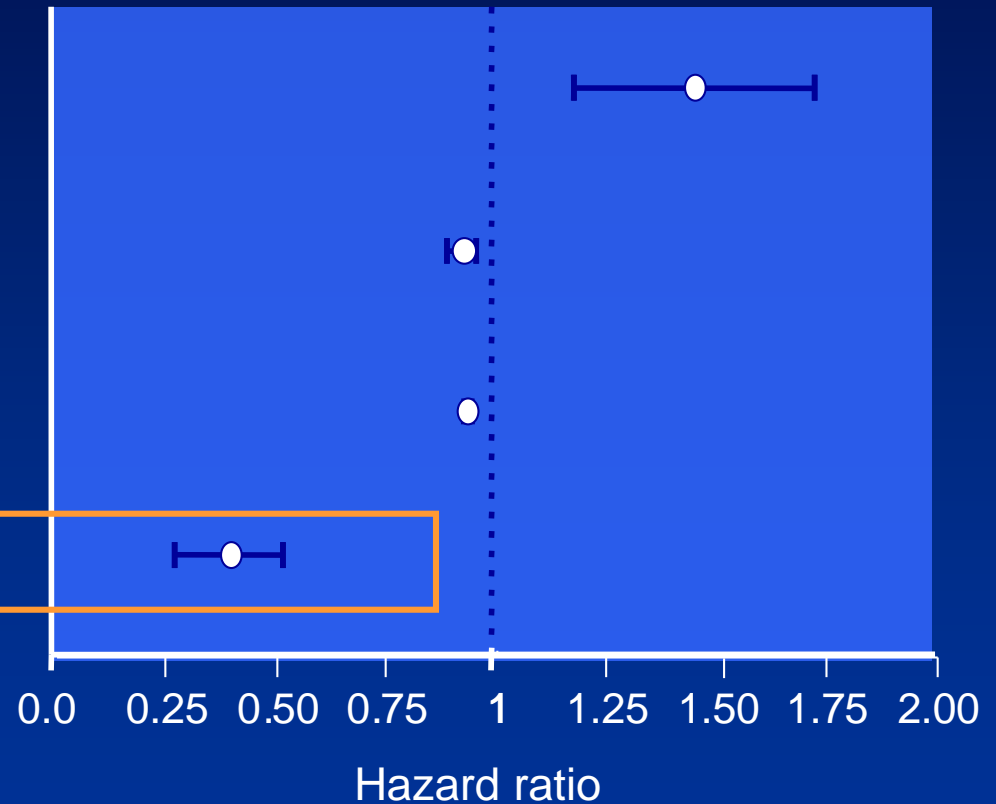
Serum Prealbumin response to renutrition

Comorbidity (+1)

Albumin d0 (+1 g/L)

Creatinine d0 (+10 $\mu\text{mol/L}$)

Δ Prealbumin d0-m3 (> 30 mg/L)



Multivariate Cox

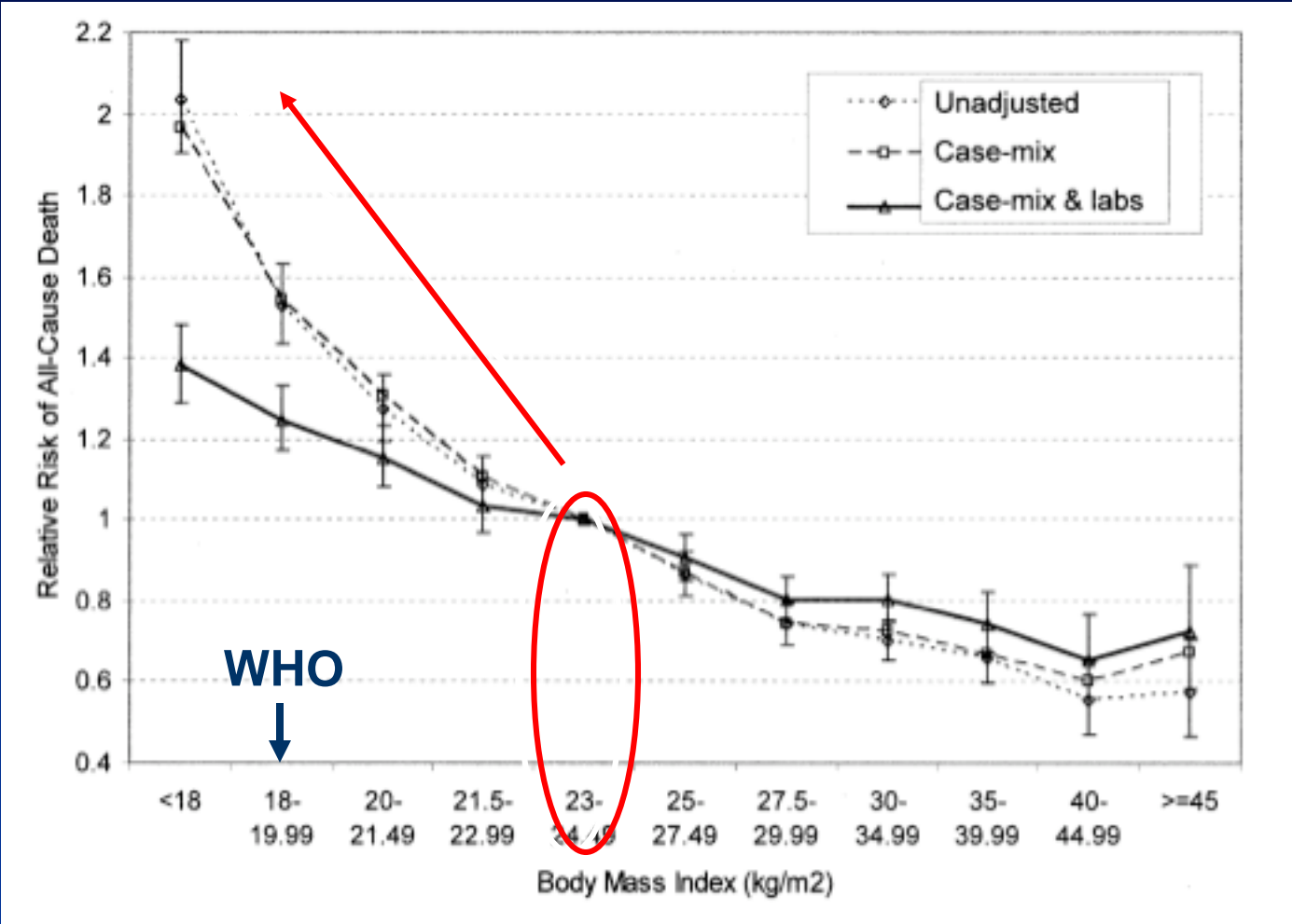
Cano et al, J Am Soc Nephrol 2007

Protein Energy Wasting - 2008

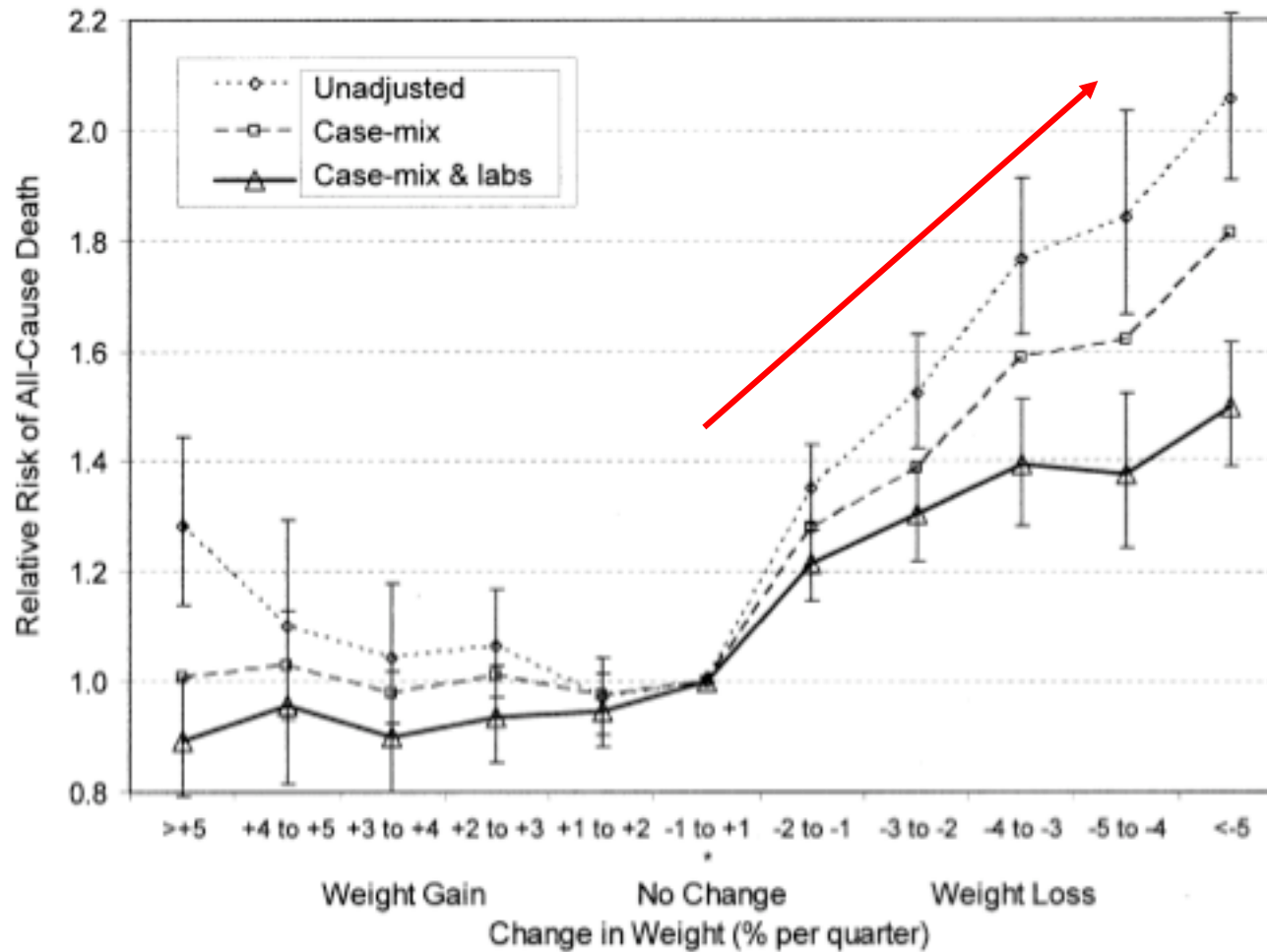
Anthropometry

- **Body Mass Index < 23** (*WHO: 18.5*)
- Gr 2 - **Weight loss > 5 %** (3 months)
- **Weight loss > 10 %** (6 months)
- **Body Fat < 10 %**

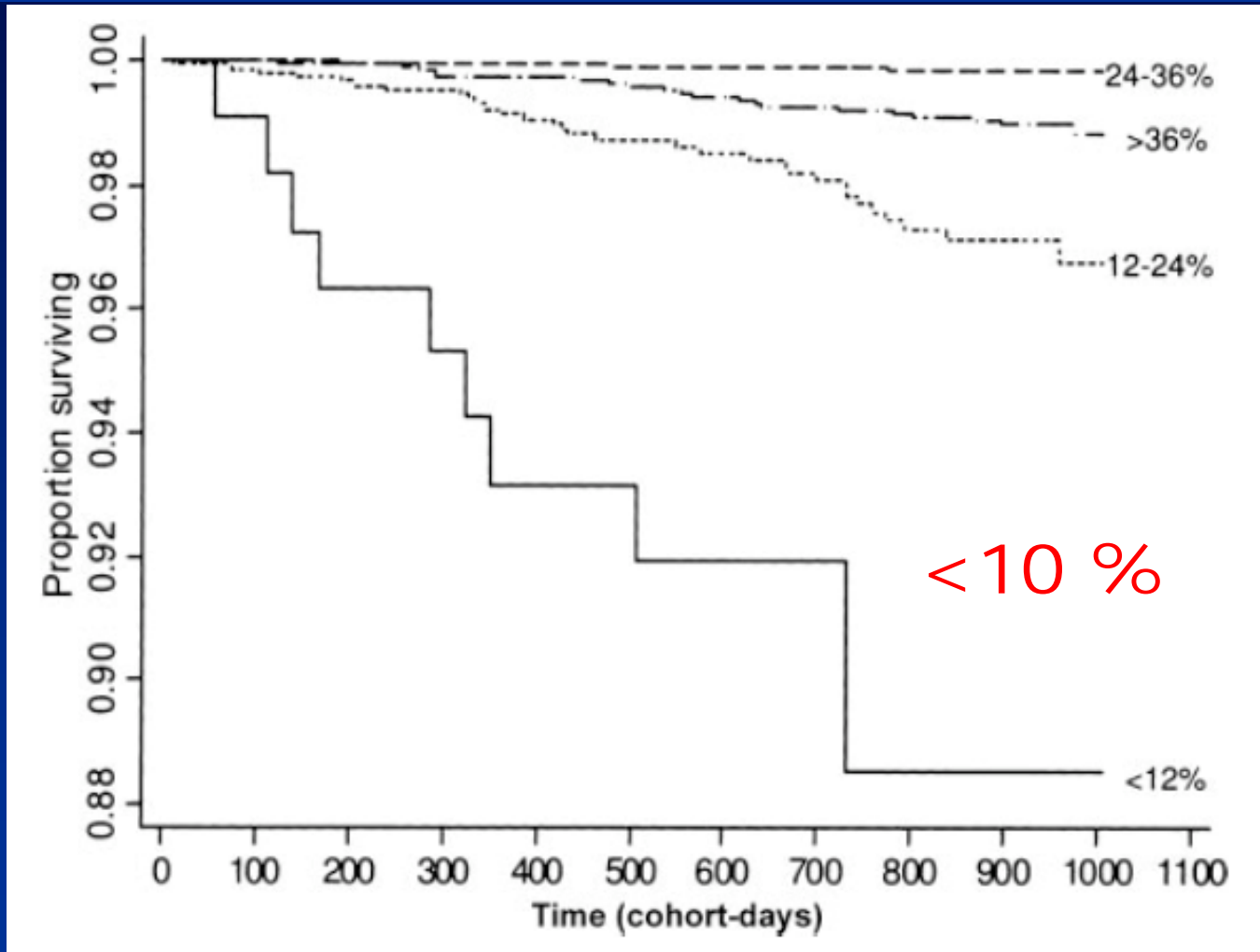
Gr 2: Body Mass Index and mortality



Weight loss and mortality



Fat Mass and mortality

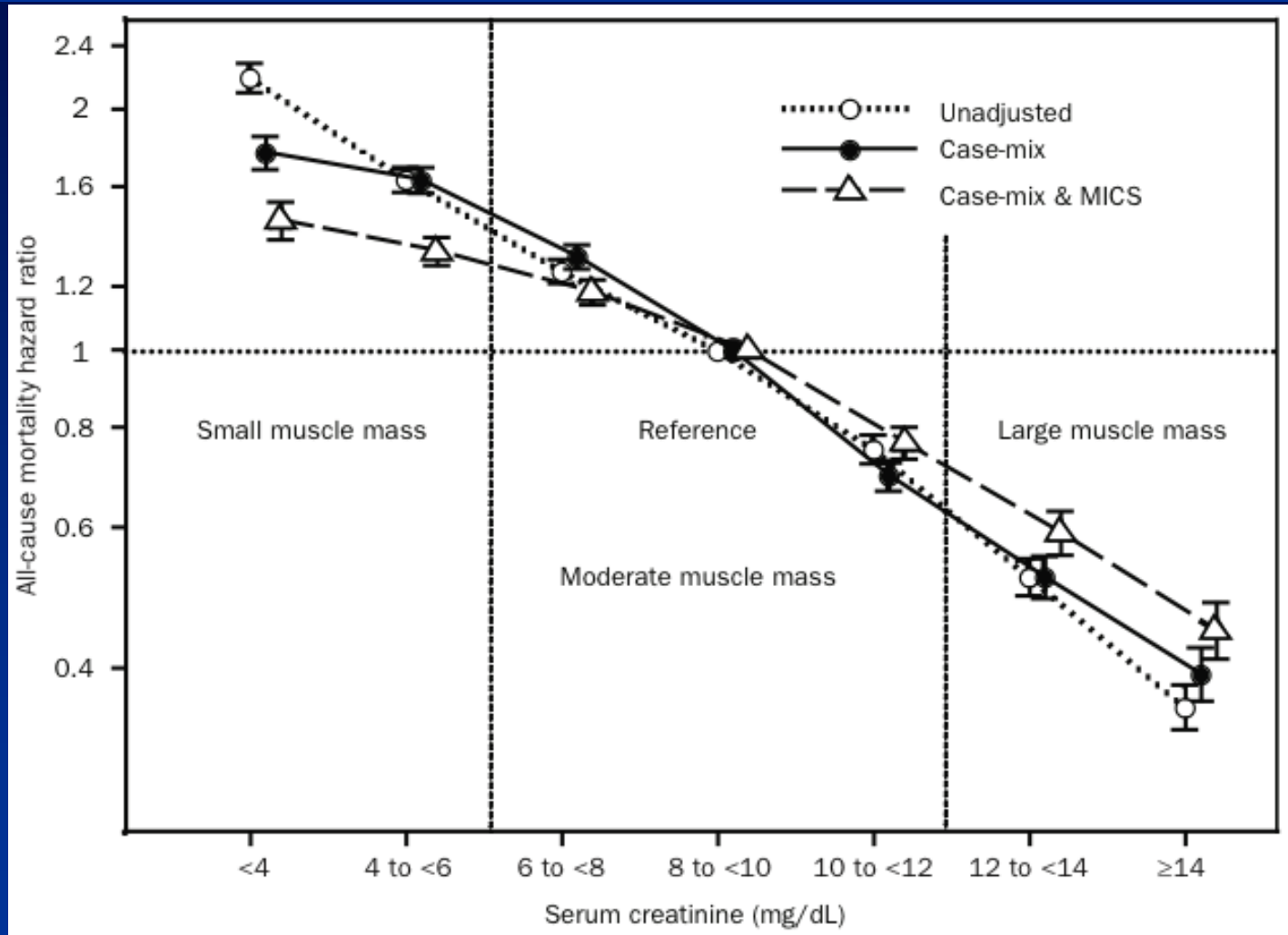


Protein Energy Wasting - 2008

Muscle

- Loss of muscle mass $> 5\%$ (3 months)
- Loss of muscle mass $> 10\%$ (6 months)
- Gr 3 - Reduced MAMC ($>10\%$ below 50th percentile)
- Predialysis S Creatinine (K-DOQIs)
- Creatinine kinetics (Garred et al.)

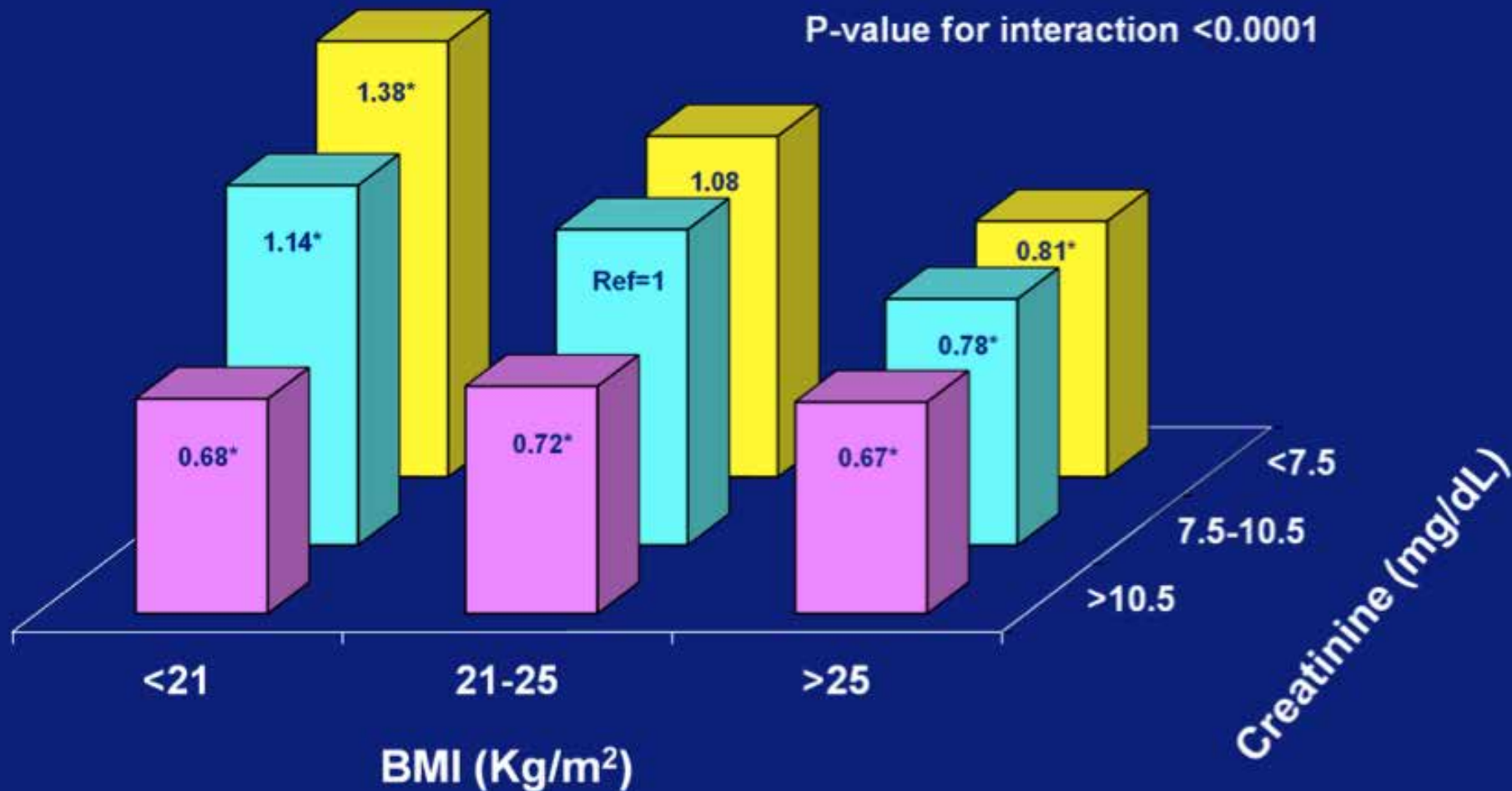
Serum Creatinine



58 000 MHD pts, retrospective 2001-06

Kalantar et al, Mayo Clin Proc 2010

Figure 2a: The relative risks of all-cause mortality due to the joint effects of BMI and creatinine



*p<0.05 as compared with the referent group; ref = referent group; BMI=body mass index
 Relative risks were adjusted for age, sex, race, vintage, 14 summary comorbidities, neutrophil/lymphocyte ratio and dialysis by catheter

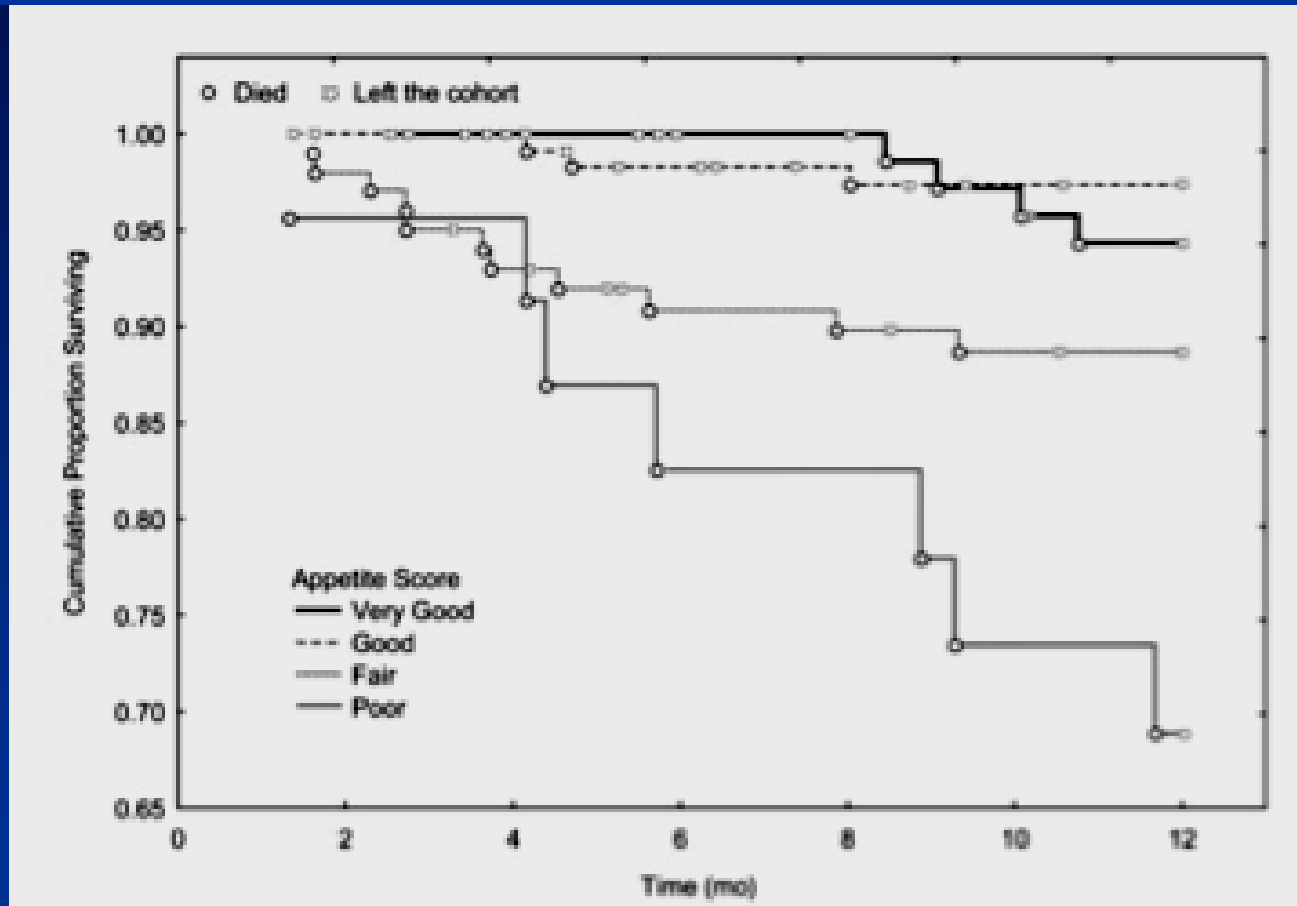


Protein Energy Wasting - 2008

Nutrients intake

- Unintentional Dietary Protein Intake
Gr 4 < 0.8 g/kg BW/day for 2 months
- Unintentional Dietary Energy Intake
< 25 kcal/kg BW/day for 2 months

Appetite: a predictor of mortality



VG

G

F

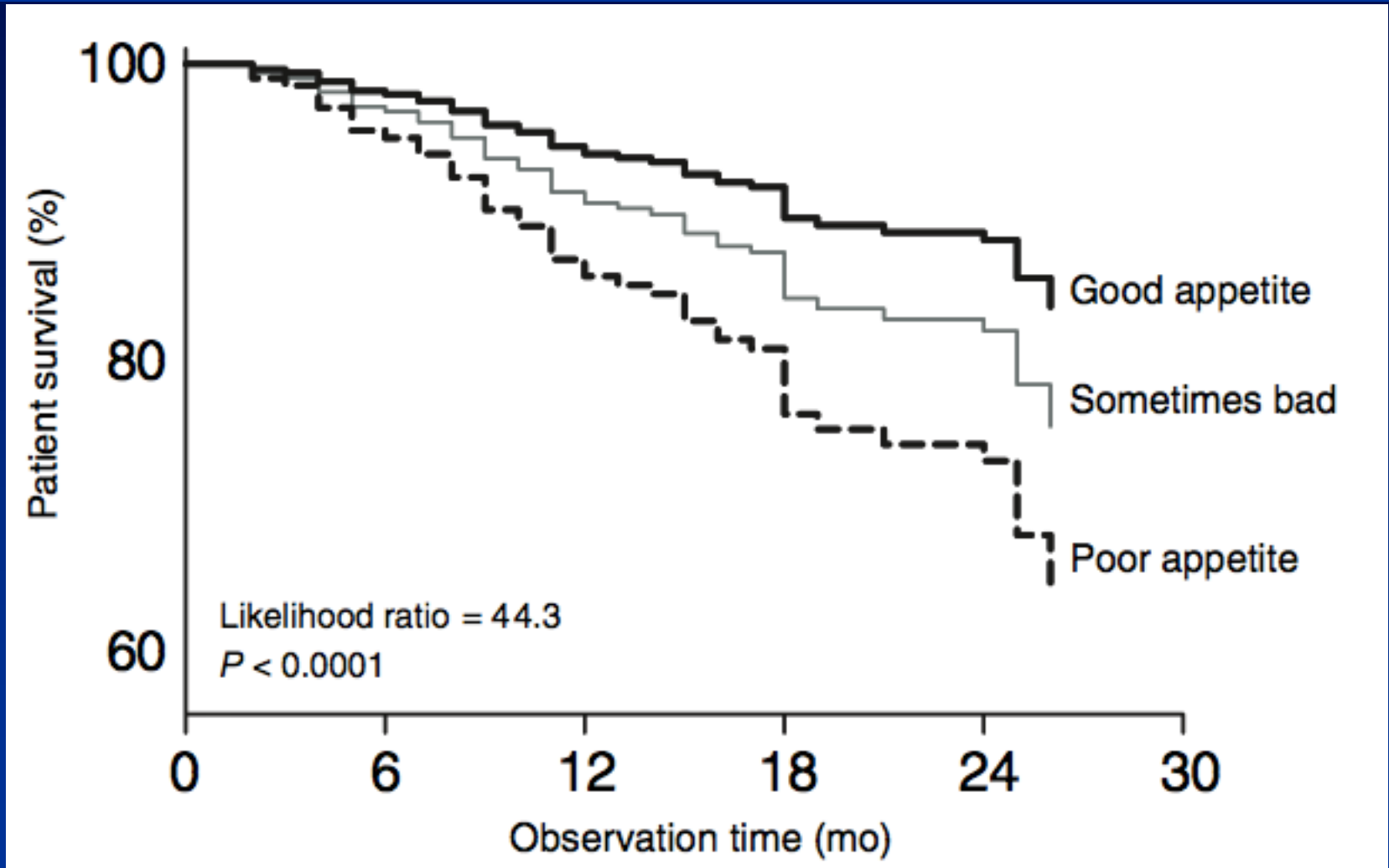
P

One year survival

331 californian MHD patients

Kalantar et al, Am J Clin Nutr 2004

Appetite and patients survival



223 swedish MHD patients

Carrero et al, Am J Clin Nutr 2007

Gr 4: Dietary intake

Protein intake

- Should be assessed monthly
- nPNA (nPCR) or food report

Energy intake

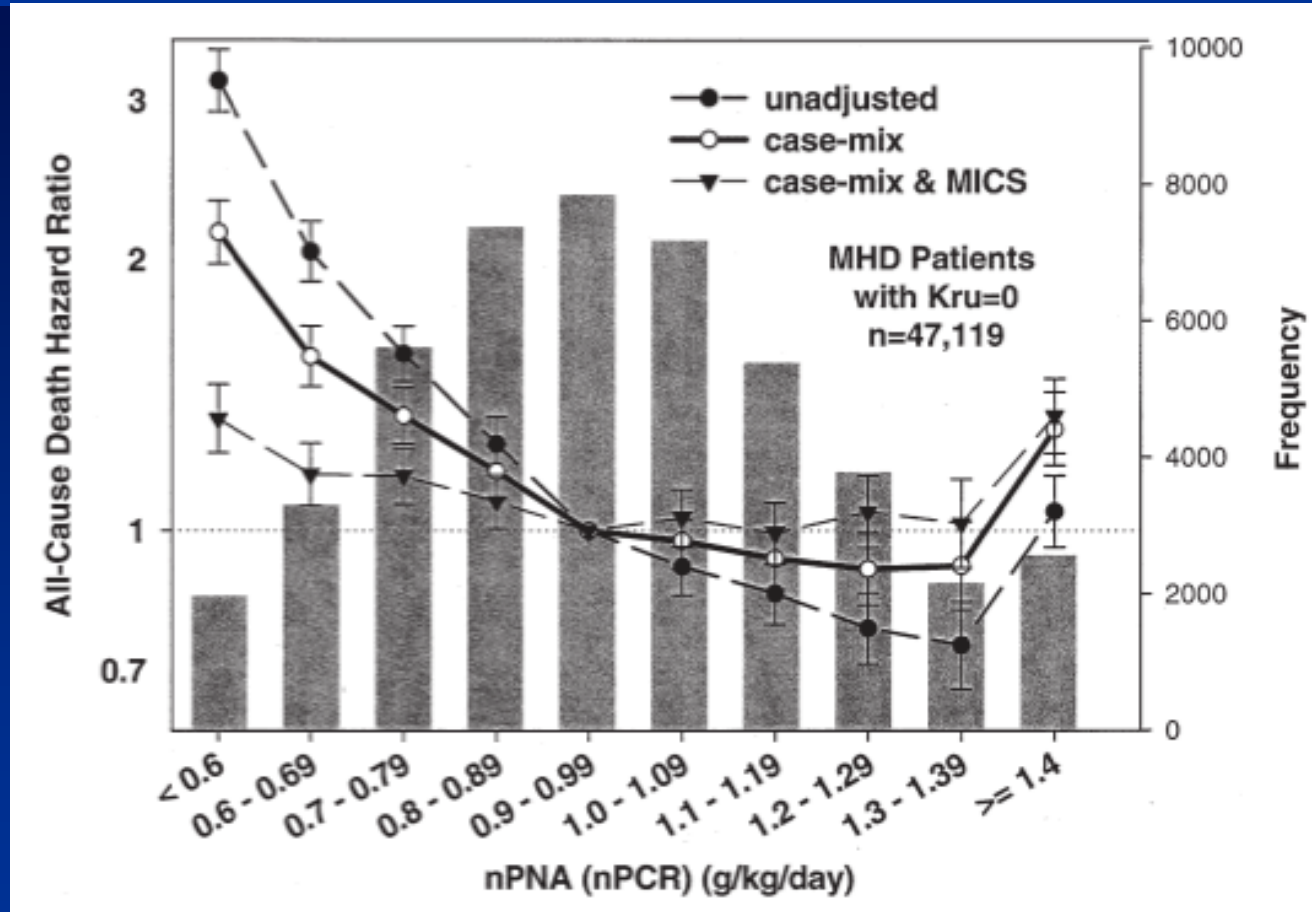
- Only by food report (every three to six month)

Gr 4: Dietary intake

- Unintentional Dietary Protein Intake
< 0.8 g/kg BW/day for 2 months
- Unintentional Dietary Energy Intake
< 25 kcal/kg BW/day for 2 months

What is the optimal protein intake ?

Mortality
RR



Defining a new predictive nutritional score

1. Which criteria

1. simple, accessible, routine
2. Include lean body mass

2. Which targets

1. Serum Albumin > 38 g/l
2. nPNA > 0.8 g/kg/day
3. BMI > 23
4. Screat/BSA > 380 $\mu\text{mol/l.m}^2$

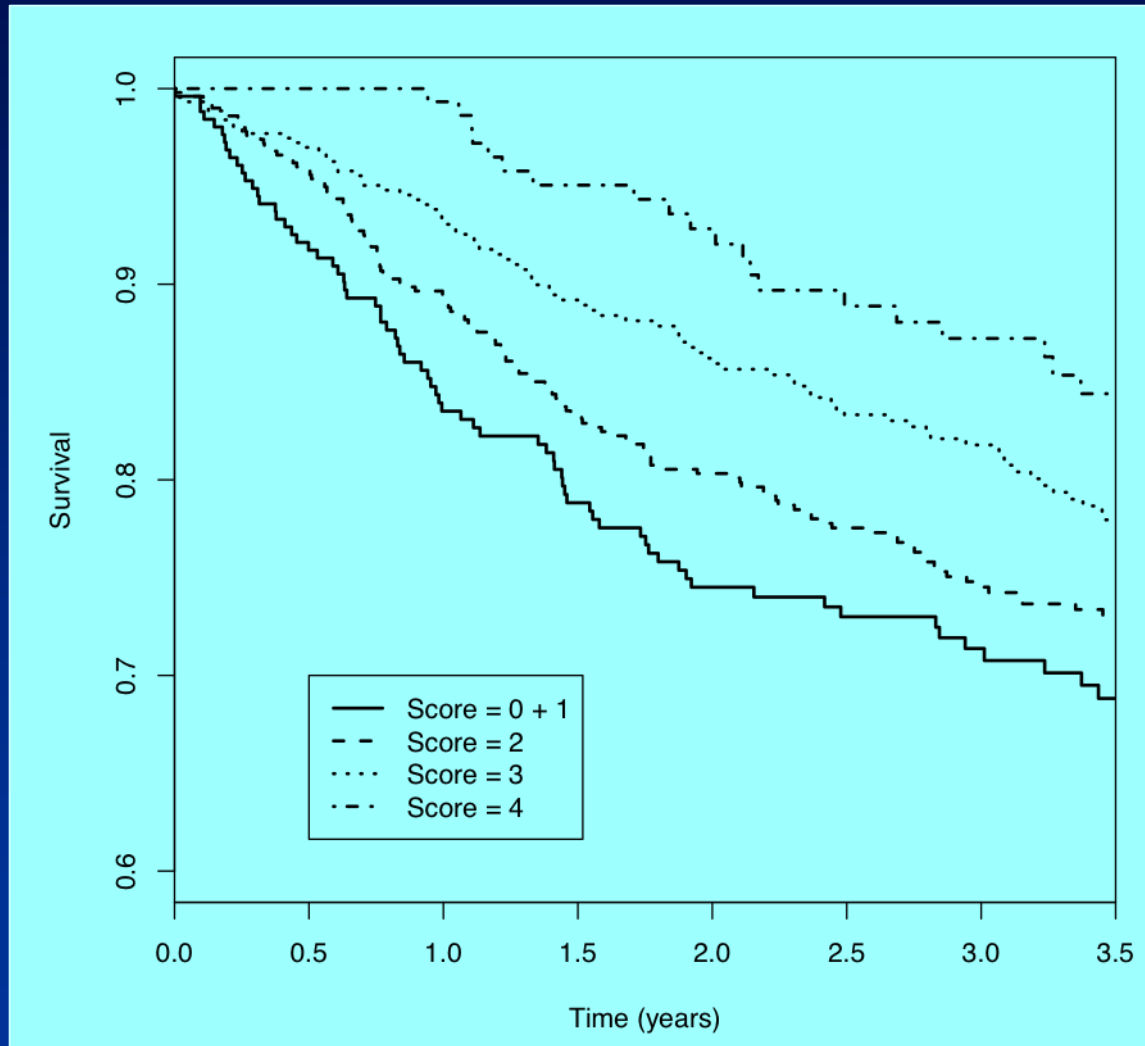
3. Calculation

0 to 4

4 : No PEW
Above all targets

0 : Severe PEW
Under all targets

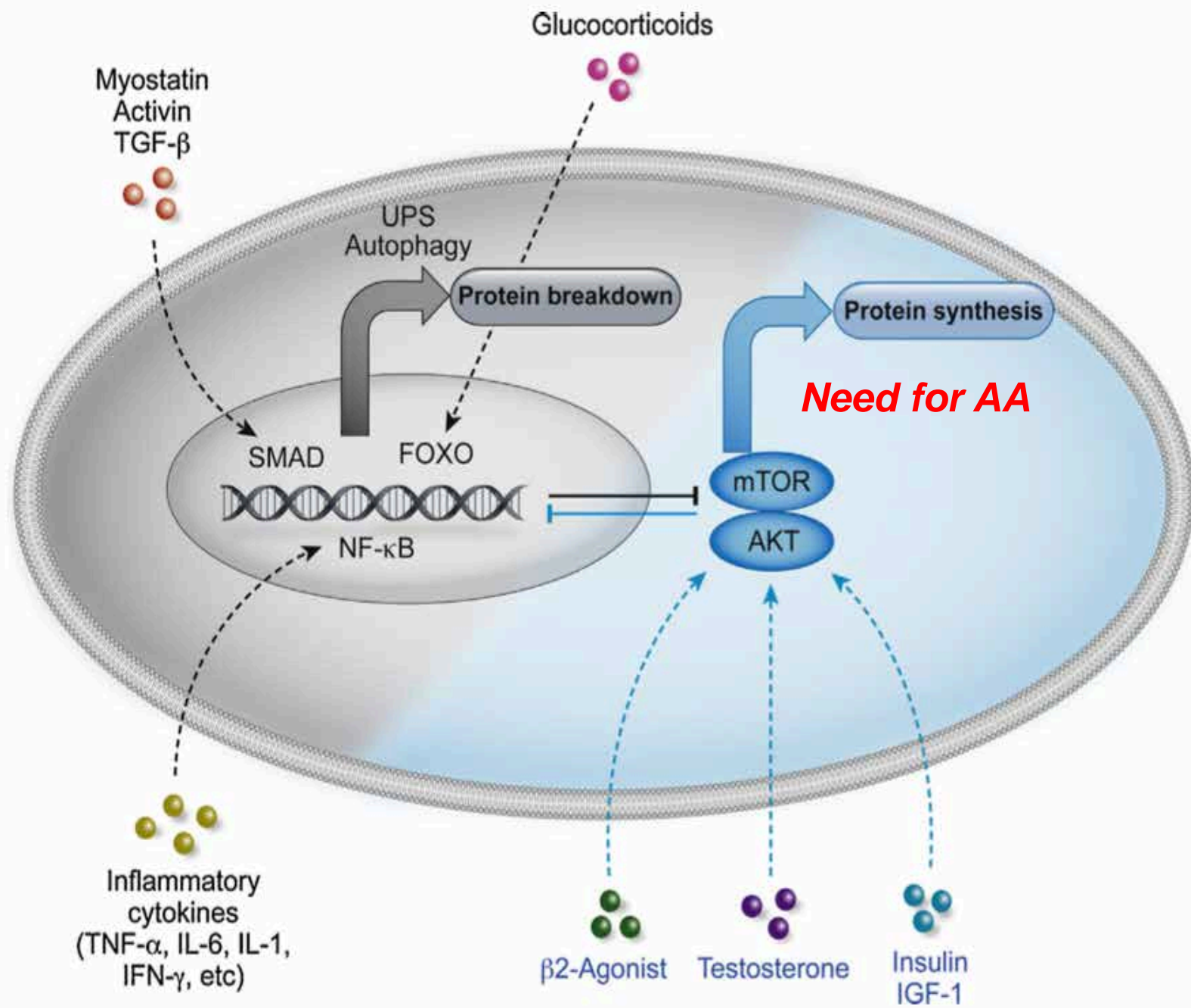
A new predictive nutritional index: Baseline



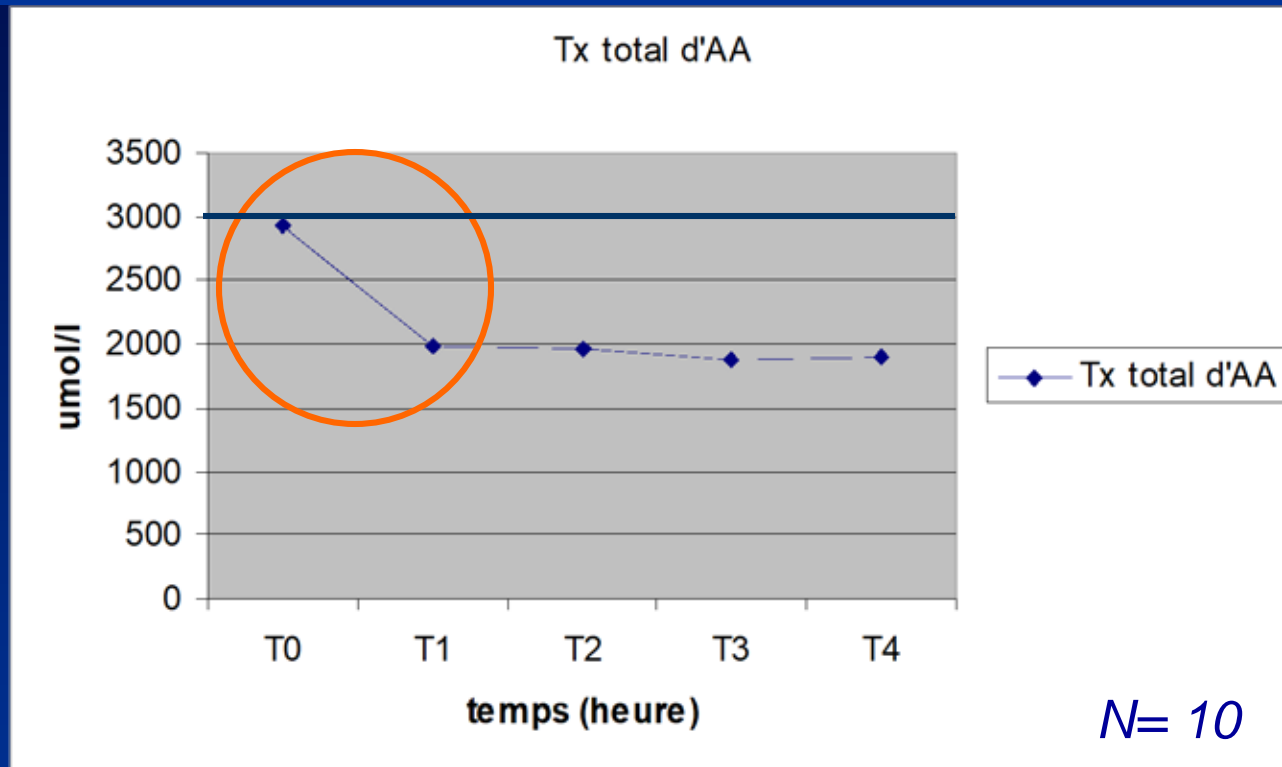
Summary

- A new terminology: Protein Energy Wasting
- A pragmatic assessment tool
- A preliminary validation in patients
- A potential useful predictive score
- Impact of nutritional disorders most powerful on patients survival

Protein Energy Wasting treatment

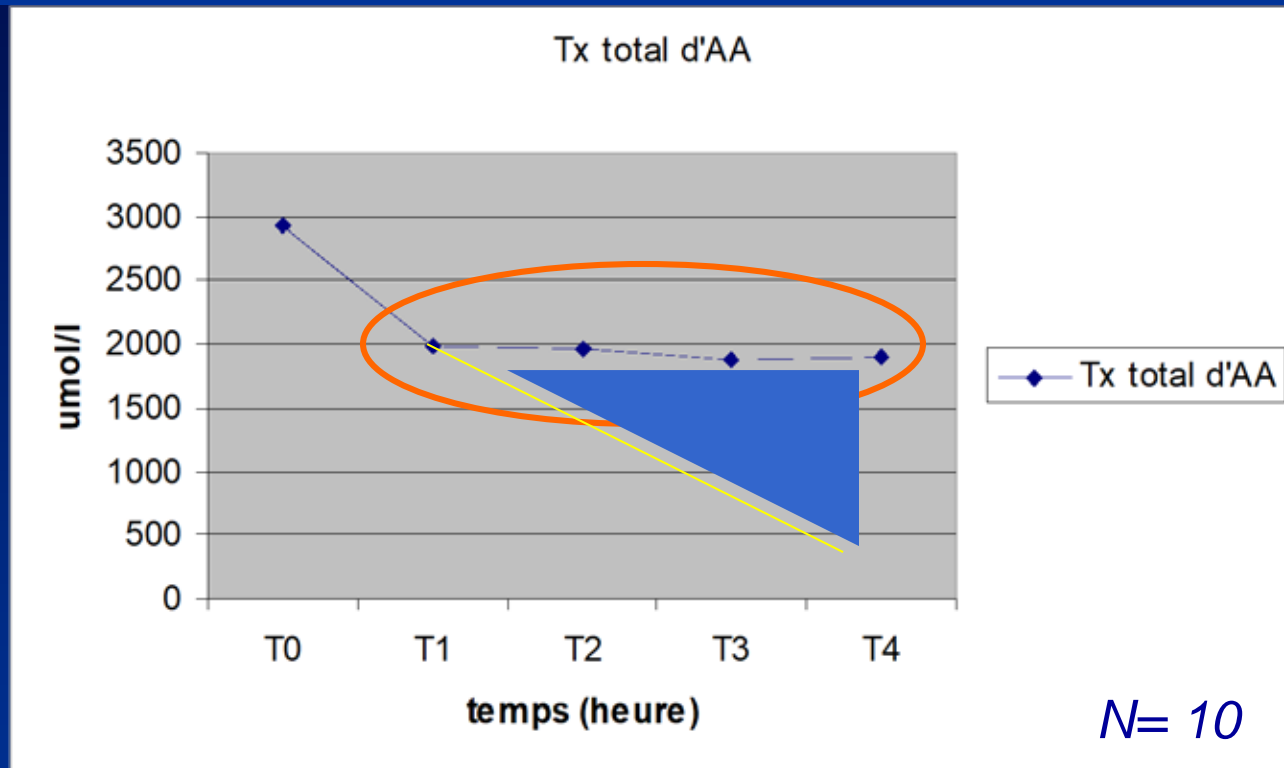


Plasma Aminoacid Profile during one Dialysis



1. The dialysis session blocks muscle protein synthesis in response to a rapid and profound decrease in plasma AA

Plasma Aminoacid Profile during one Dialysis



Muscle protein catabolism occurs in order to maintain plasma amino acids

PEW treatment

1. Oral- Enteral support
2. Intradialytic nutrition (IDPN)
3. Androgens

Per Dialytic Oral Supplement

1. Oral supplement during the EER session
2. Every 30 min (enriched yoghurt)
3. Total: 0.6 g prot/kg + 15 kcal/kg (45 g prot, 1125 kcal)



1050 kcal x3/week = 450 kcal/d

Per Dialytic Oral Supplement

Plasma Amino acids

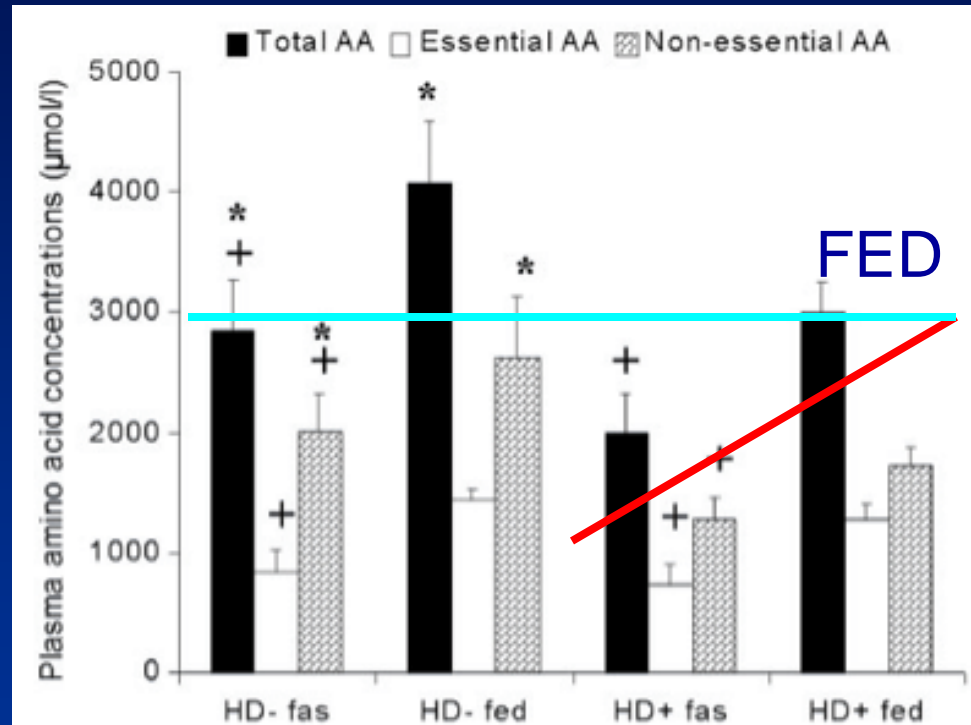


Fig. 3. Concentrations of total, essential, and nonessential amino acids in plasma in the steady-state periods in all study protocols. +Significant difference in amino acid concentration during fasting compared with feeding. *Significant difference in amino acid concentration during the HD+ protocol compared with the same condition (fasting or feeding) during the HD- protocol.

Per Dialytic Oral Supplement

Nitrogen Balance

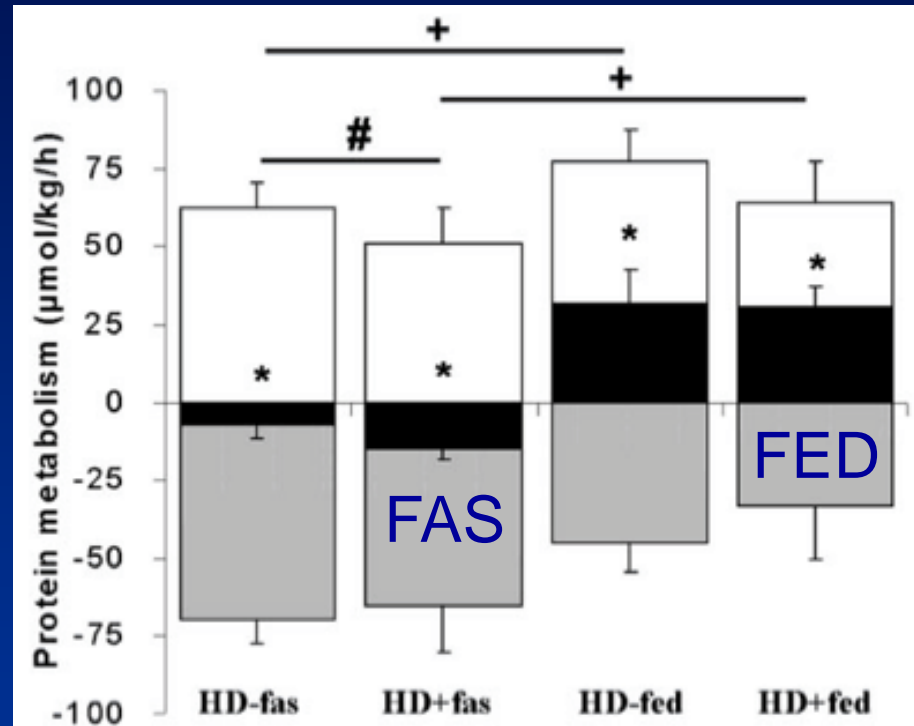


Fig. 5. Summary of whole body protein breakdown (gray bars), synthesis (open bars), and protein balance (filled bars) under all experimental conditions. *Whole body protein balance significantly different from 0. +Whole body protein balance significantly different between fasting and feeding. #Whole body protein balance significantly different between the HD+ and HD- protocols.



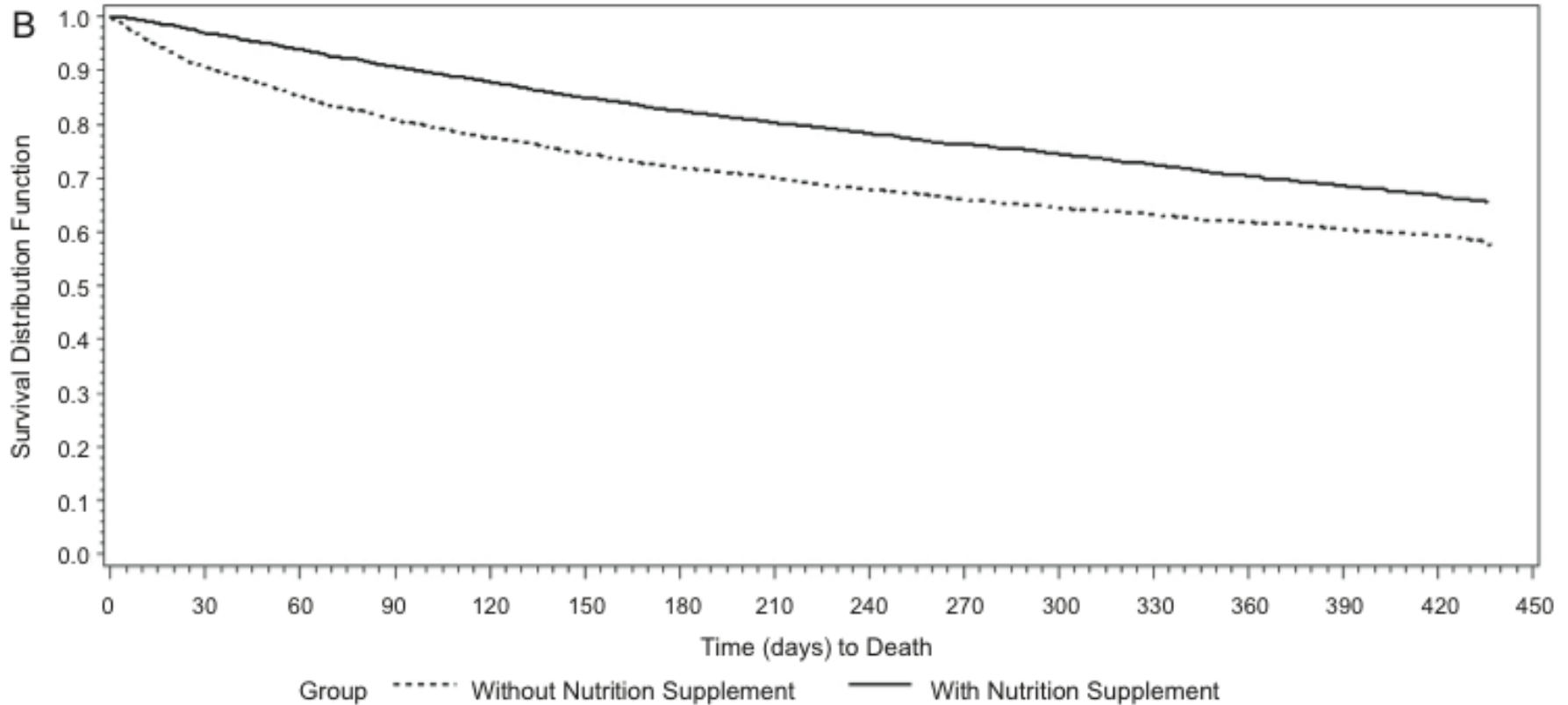
Oral-enteral nutrition: long term

Case control study 2007-2009, FMC cohort, USA
5000 pts receiving Oral supplement vs 5000 controls
S Alb < 35 g/L
One supplement during the session
One year, 156 food supplements

Table 1. Oral Nutritional Supplement Product Choices

Nutrition Product	Serving Size	Protein (g)	Calories
NeproCarb Steady	8 fl oz	19	425
ProStat RC	1 fl oz	15	60
ZonePerfect	50-g bar	14	210
VitalProteinRX	60-g bar	20	210

Oral-enteral nutrition: long term



Parenteral Support

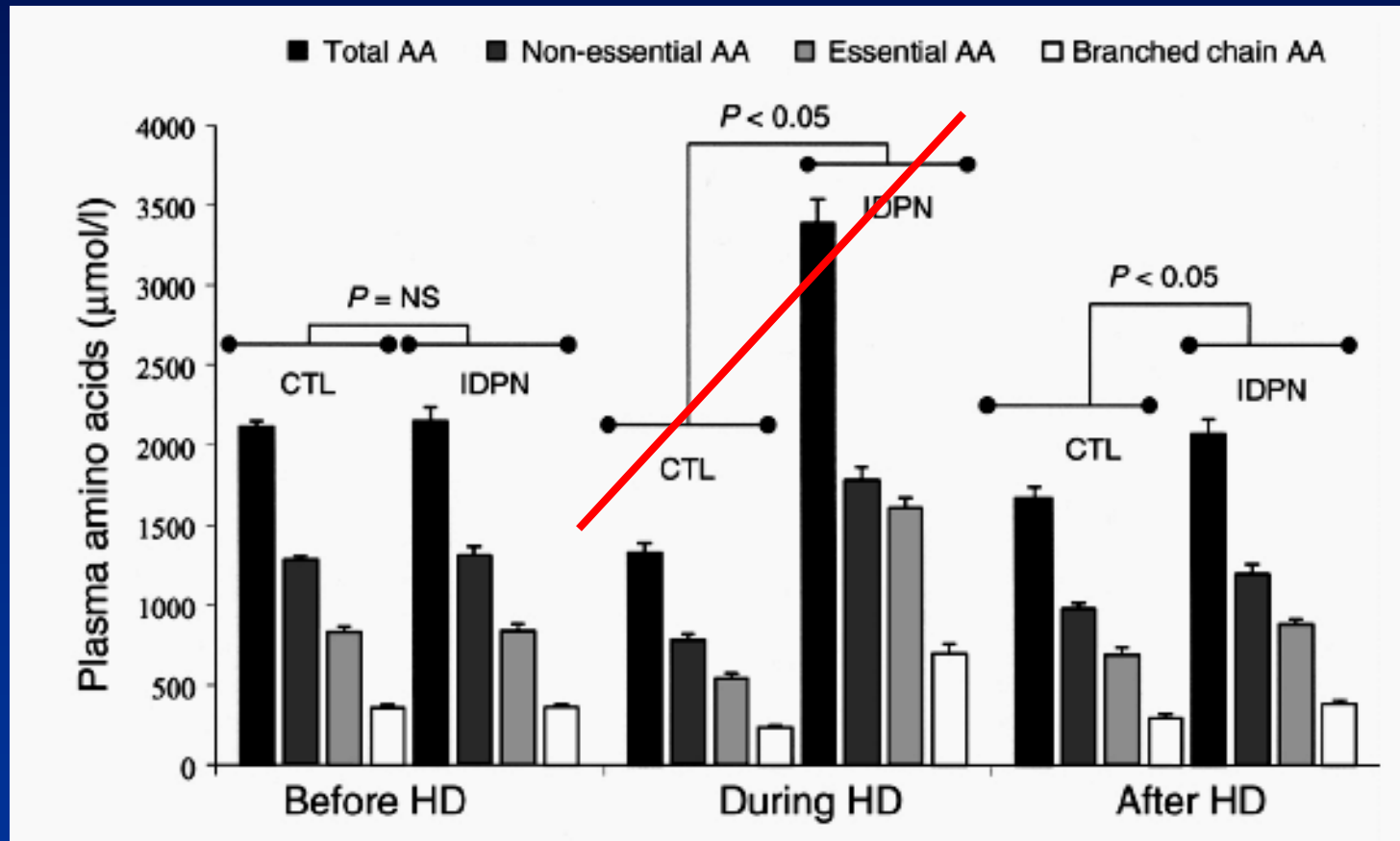
IntraDialytic Parenteral Nutrition

IDPN standard solution

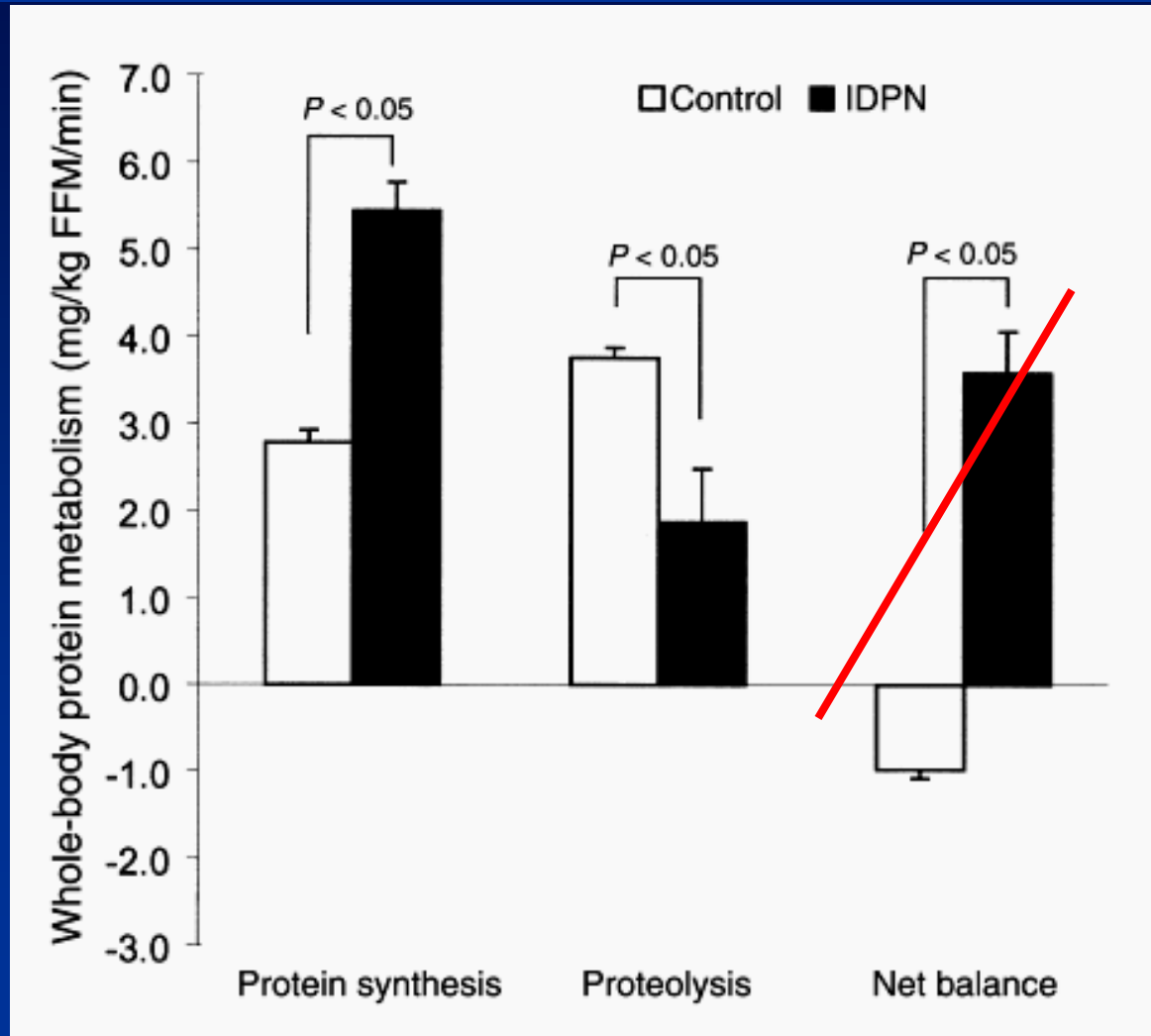
1. 600 ml (300 ml AA 15%, 150 ml IL20%, 150 Gluc 50%)
2. 150 ml/hr
3. 190 kcal/hr

700-1000 kcal x3/week = 350 - 450 kcal/d

IDPN: Plasma amino acids



IDPN: Whole Body Protein Metabolism



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Randomized control trials

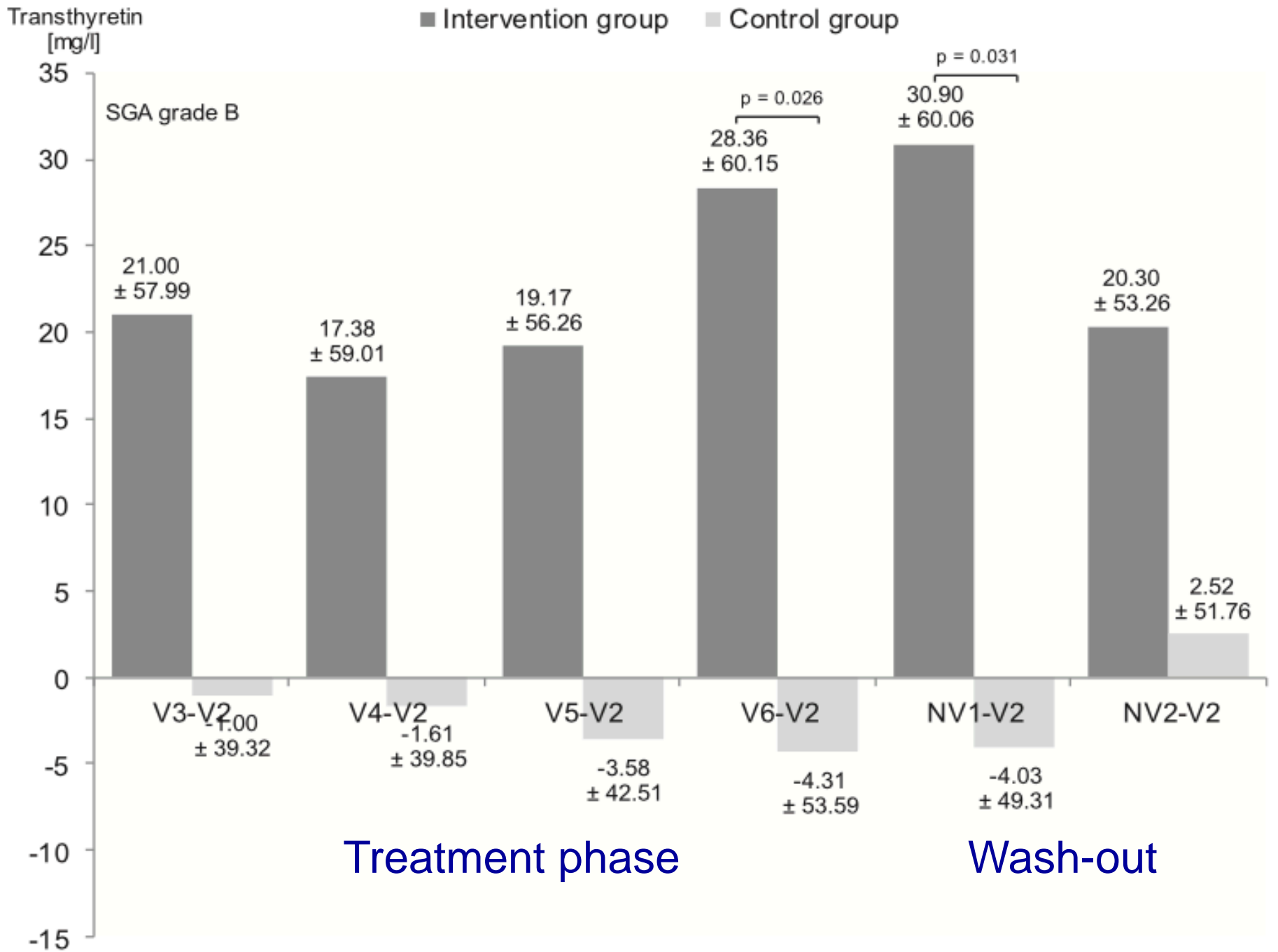
Intradialytic parenteral nutrition in maintenance hemodialysis patients suffering from protein-energy wasting. Results of a multicenter, open, prospective, randomized trial[☆]

Tobias A. Marsen ^{a,*}, Justinus Beer ^b, Helmut Mann ^c, for the German IDPN-Trial group

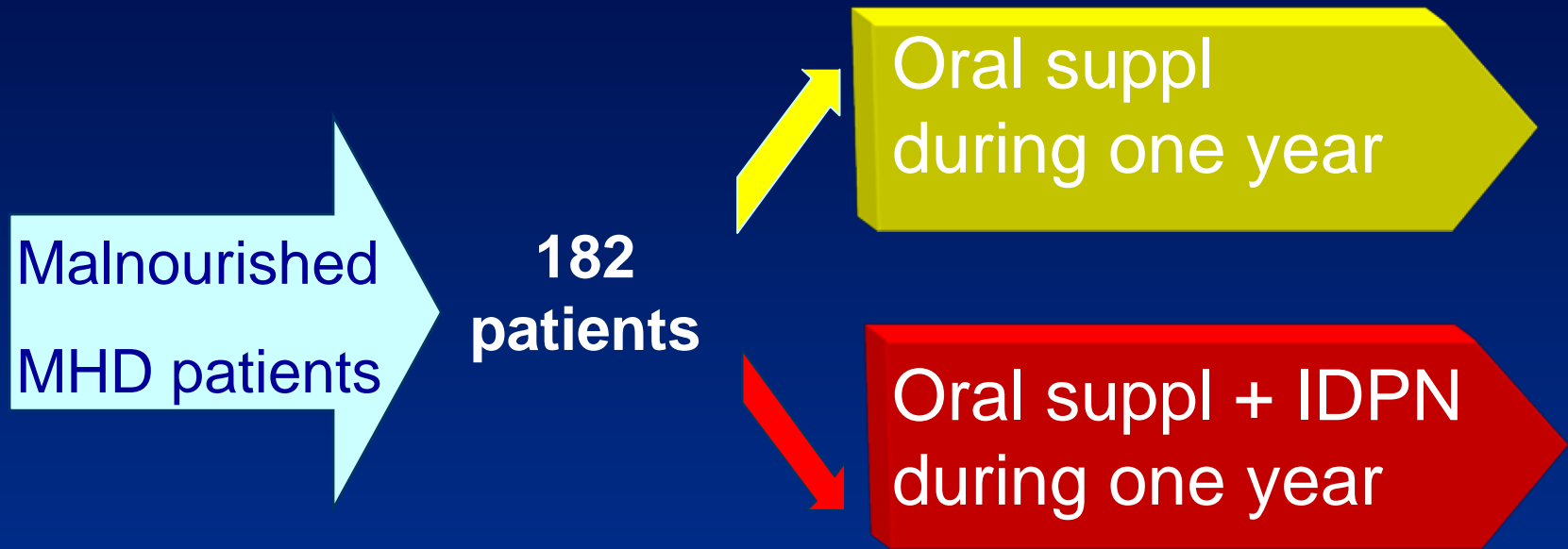
- RCT in 107 MHD pts in Germany
- 4 months treatment followed by 3 months w/o treatment

Glucosteril [®] 70% ^a	1.35 ± 0.36 g
Aminoven [®] 15% ^a	0.68 ± 0.13 g
Lipovenous [®] MCT 20% ^a	0.47 ± 0.13 g
Omegaven-Fresenius ^{®a}	0.07 ± 0.02 g
FrekaVit [®] , water soluble ^a	10 mL
Tracitrans plus ^{®a}	10 mL
Nefrocarnit ^{®b}	1 g
	13.59 ± 3.27 kcal
	10.81 ± 2.83 kcal
	10.29 ± 3.96 mL

Dose/kg/session x 3/wk



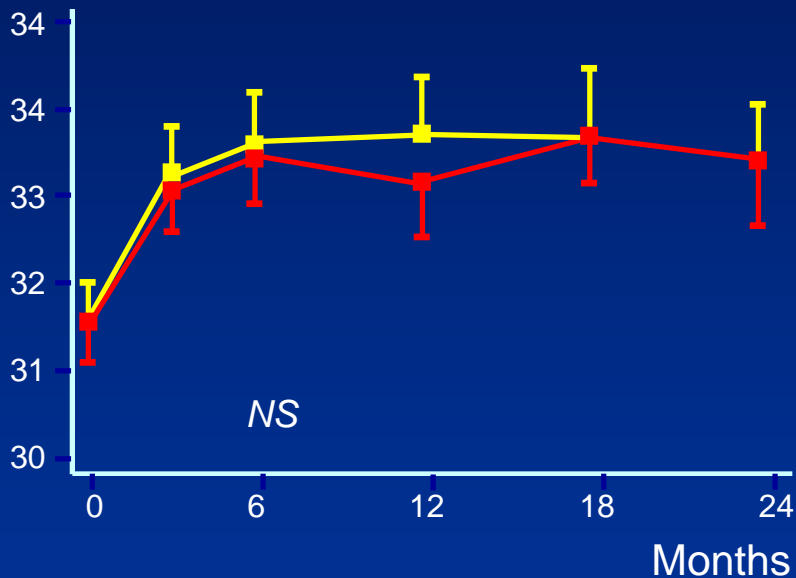
FineS design



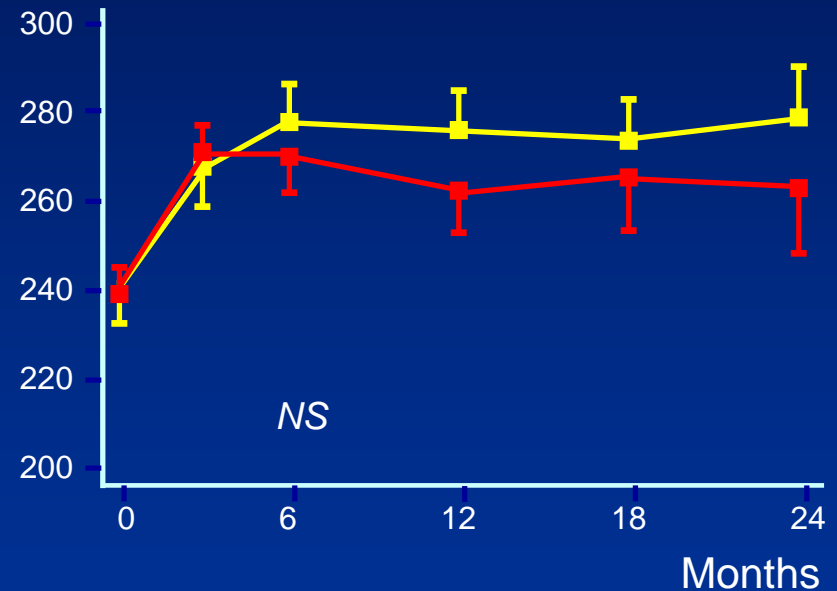
- Follow-up: two years (treatment period + one year)
- Visits at day 0 and month 3, 6, 12, 18 and 24

Effects of Enteral and IDPN Support

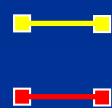
Serum albumin, g/L



Serum prealbumin, mg/L



Control group
IDPN group



Nutritional Education vs Oral supplement

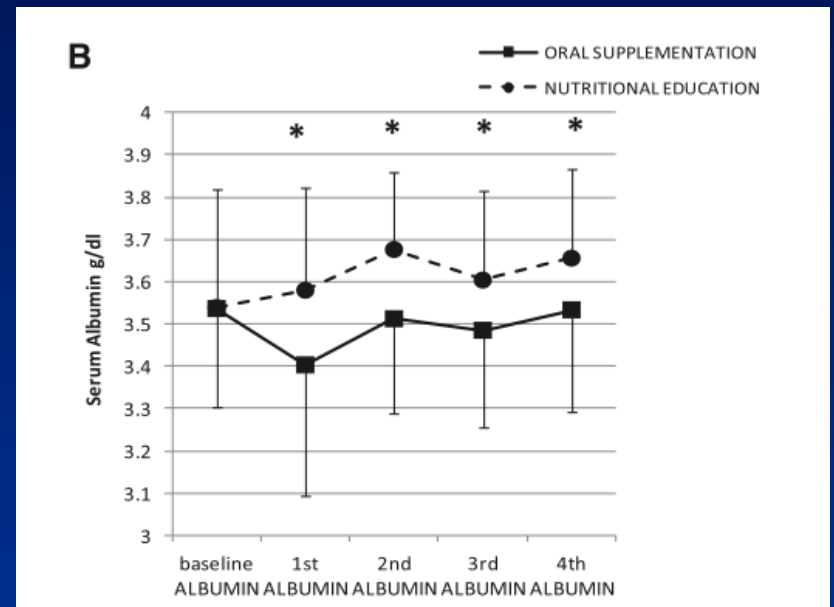
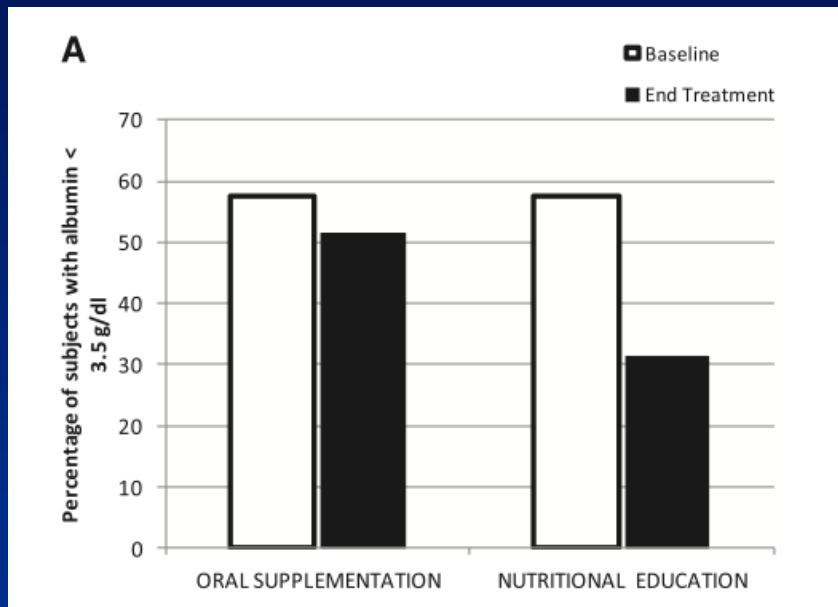
120 MHD pts from Spain

RCT: Nutritional Education program vs Oral supplement for 4 months

Nutritional Education program: 12 sessions of nutritional knowledge and culinary recommendations and balanced menus

Oral supplement: Nepro®, 470 ml/session 3x / wk

Effects on PEW and S Albumin



Growth factors- orexigens

- Growth hormone and IGF-1
- Ghrelin
- Androgens

Effects of Ghrelin in malnourished MHD

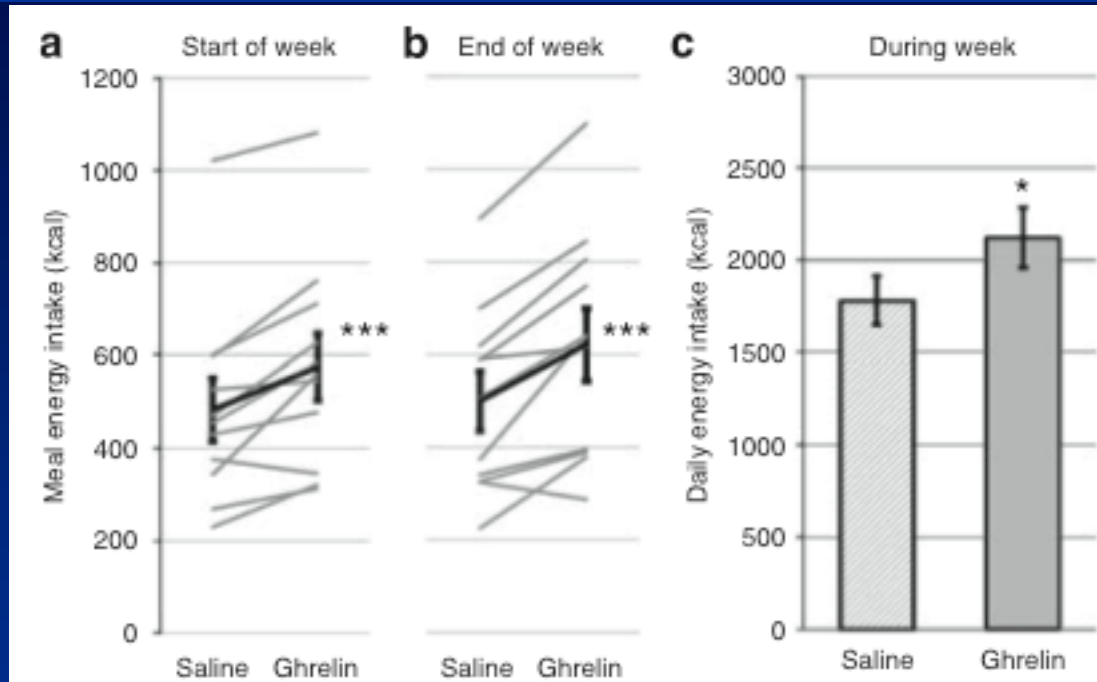
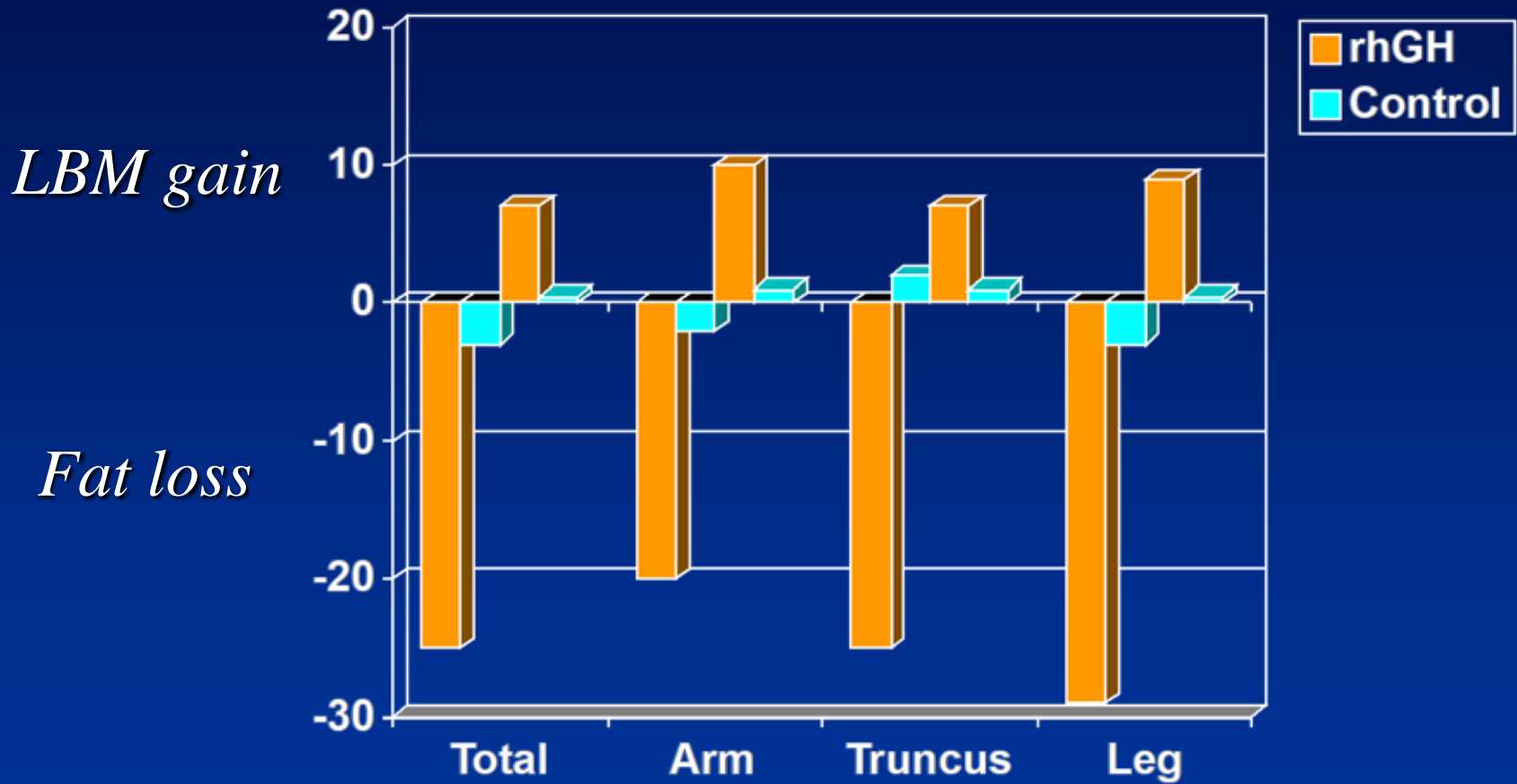


Figure 2 | Energy intake with saline compared with ghrelin. (a) Study meals at the start of saline and ghrelin weeks showing an increase in energy intake after the first injection (individual values and mean \pm s.e., $P < 0.001$); (b) study meals at the end of saline and ghrelin weeks showing persistence of the increase in energy intake ($P < 0.001$); and (c) food diaries during both weeks showing a consistent effect throughout the diurnal period (mean \pm s.e., $P = 0.040$). * $P < 0.05$; *** $P < 0.01$.

RhGH Treatment in MHD Patients: Segmental Body Composition (DEXA)

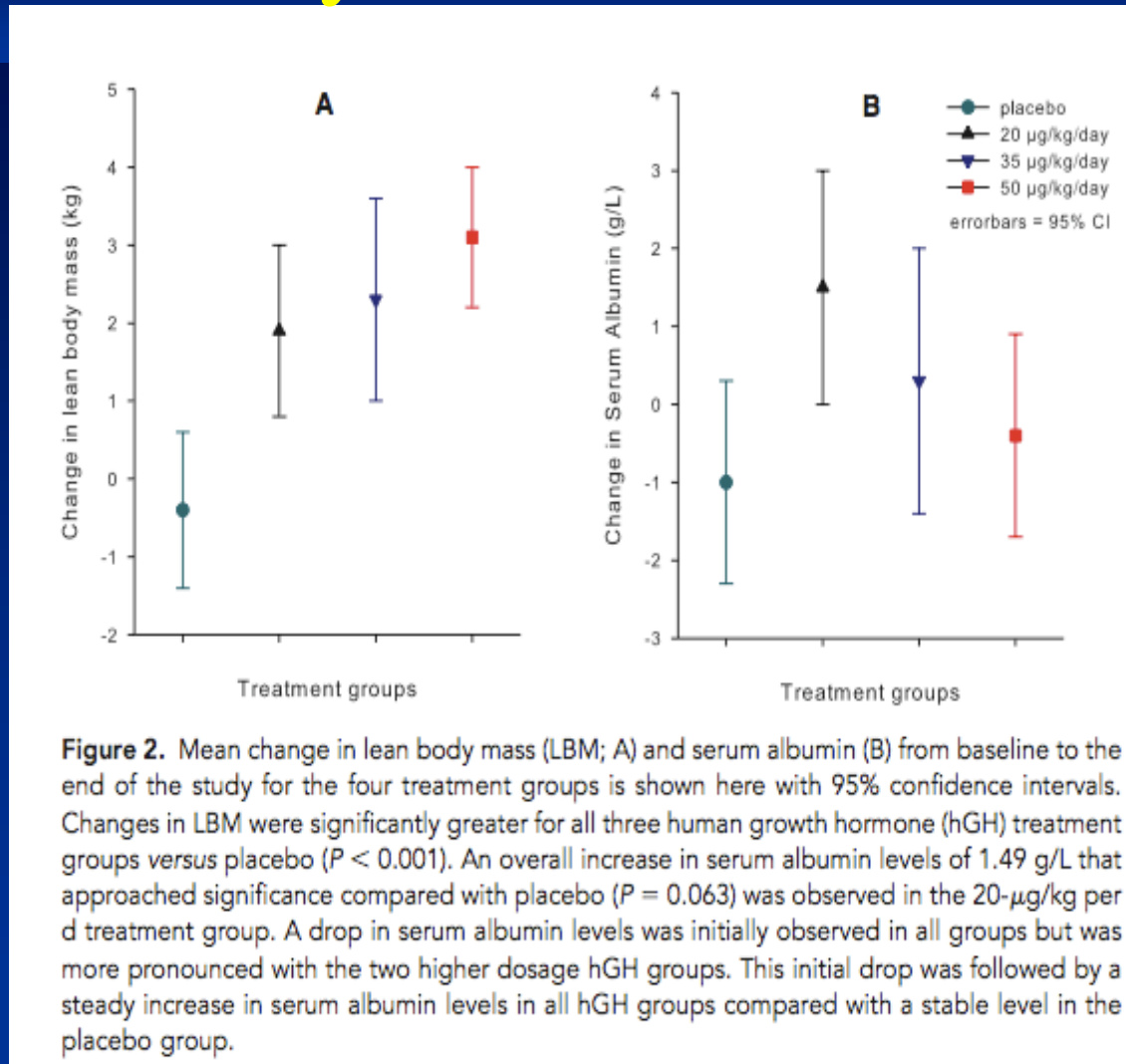


Growth Hormone Treatment during Hemodialysis in a Randomized Trial Improves Nutrition, Quality of Life, and Cardiovascular Risk

Bo Feldt-Rasmussen,* Martin Lange,[†] Wladyslaw Sulowicz,[‡] Uzi Gafer,[§] Kar Neng Lai,^{||} Jonas Wiedemann,** Jens Sandal Christiansen,[¶] Meguid El Nahas;^{††} and the Adult Patients in Chronic Dialysis (APCD) Study Group

*Department of Nephrology, Copenhagen University Hospital, Copenhagen, Denmark; [†]Novo Nordisk Inc, Princeton, New Jersey; [‡]Department of Nephrology, Jagiellonian University, Krakow, Poland; [§]Department of Nephrology and Hypertension, Rabin Medical Center, Petah Tikva, Israel; ^{||}Department of Medicine, University of Hong Kong, Hong Kong; [¶]Department of Endocrinology and Diabetes, Århus University Hospital, Århus, Denmark; **Novo Nordisk A/S, Bagsvaerd, Denmark; and ^{††}Sheffield Kidney Institute, Northern General Hospital, Sheffield, United Kingdom

Lean Body Mass Serum Albumin

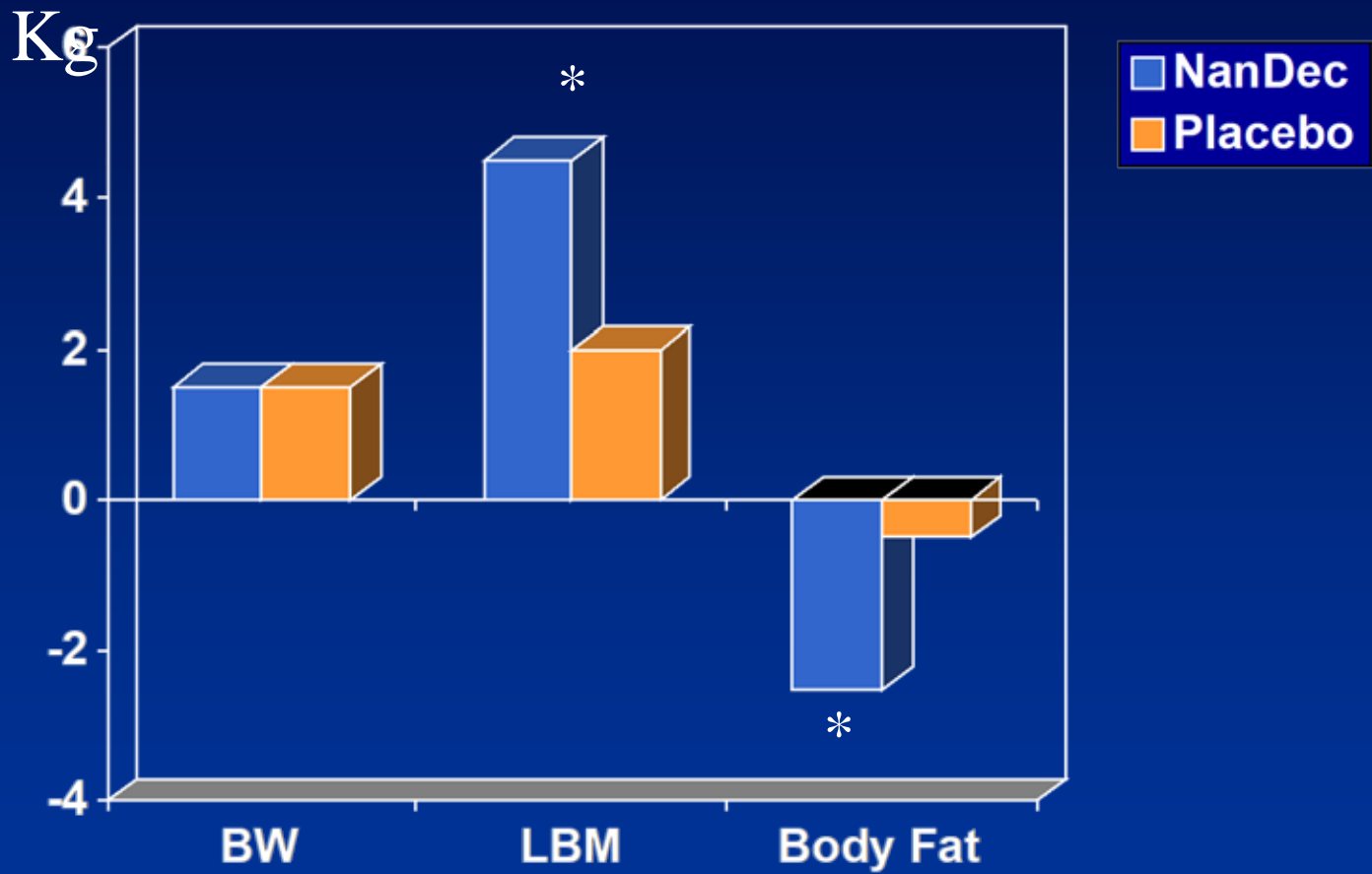


Anabolic Factors: Androgens

Anabolic Factors: Androgens

1. In case of severe malnutrition resistant to optimal nutritional intervention, a course of androgens should be proposed in MHD patients for three to six months (Evidence level II)
2. Androgens should be administered weekly or bimonthly (Evidence level II)
3. Patients should be monitored at regular intervals for side effects (hirsutism, voice change, priapism, alteration in plasma lipids, liver tests and prostatic markers) (Evidence level II)
4. Patients with a known prostate cancer should not receive androgens (Evidence level II)

Androgens Treatment in MD Patients: Body Composition (DEXA)



Johansen et al, JAMA 1999

Androgens Treatment in MD Patients: Functional status and well-being

- Improvement in Treadmill time (+20% vs -28%)
- Increase in Maximum work output (+21% vs -35%)
- Reduction in Stair climbing time (-9% vs +8%)
- Reduction in Fatigue index (Profile of Mood States) (-50% vs +36%)

Johansen et al, JAMA 1999

Conclusion

Nutritional supplements: Oral / intravenous - limited

Nutritional education: it works !

Growth factors: many reasons - not enough evidence

Androgens: a possible short-term use in severe case