

ALTERAZIONI DEL METABOLISMO CALCIO-FOSFORO E DIETA IPOPROTEICA

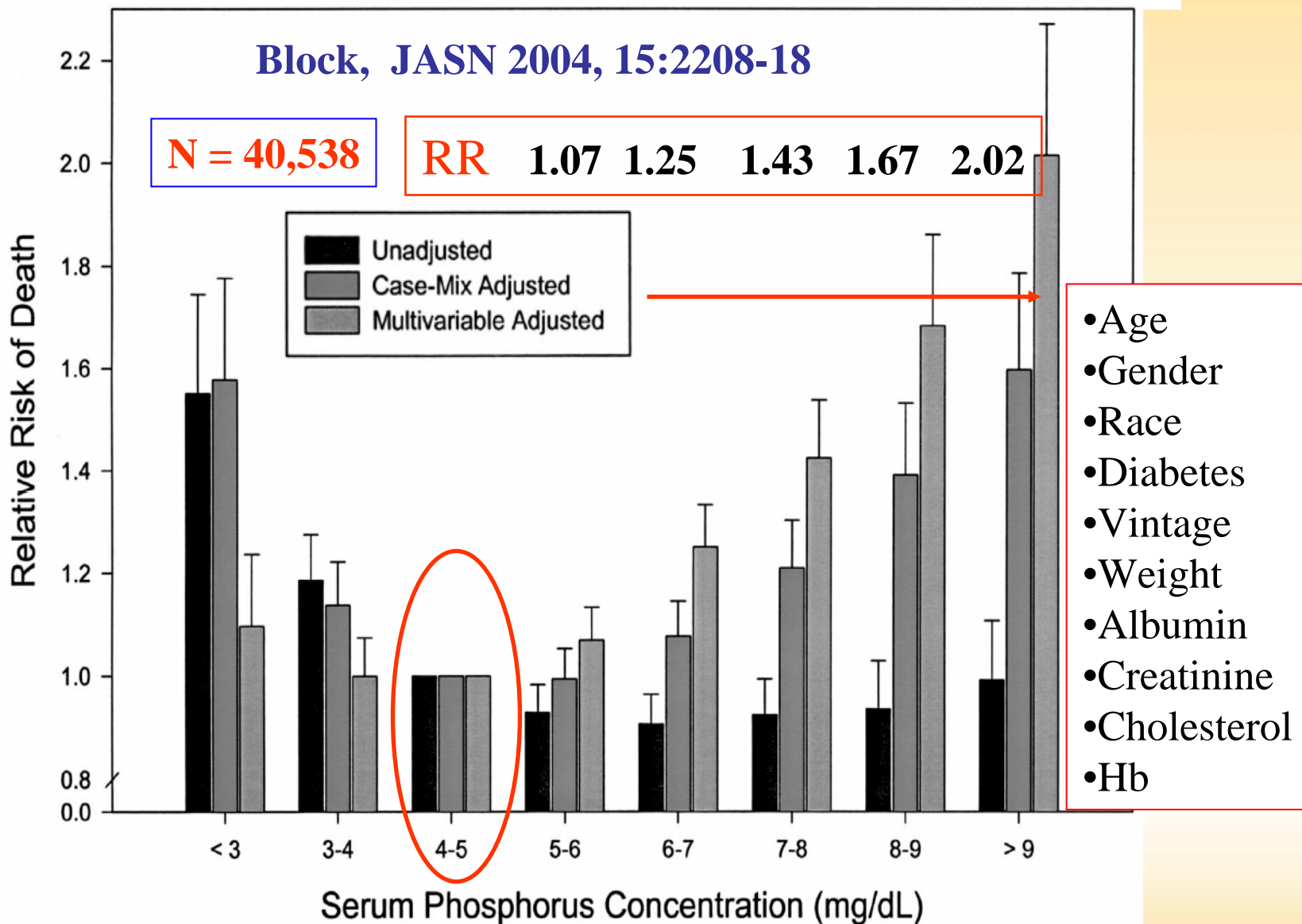
Fabio Malberti

*Divisione di Nefrologia e Dialisi
Cremona*

AGENDA

- **Fosforemia e mortalità**
- **Fosforemia e progressione IR**
- **Target di fosforemia nei vari stadi di CKD**
- **Quali dati nella realtà clinica**
- **Effetti clinici della restrizione dietetica**
- **Raccomandazioni**

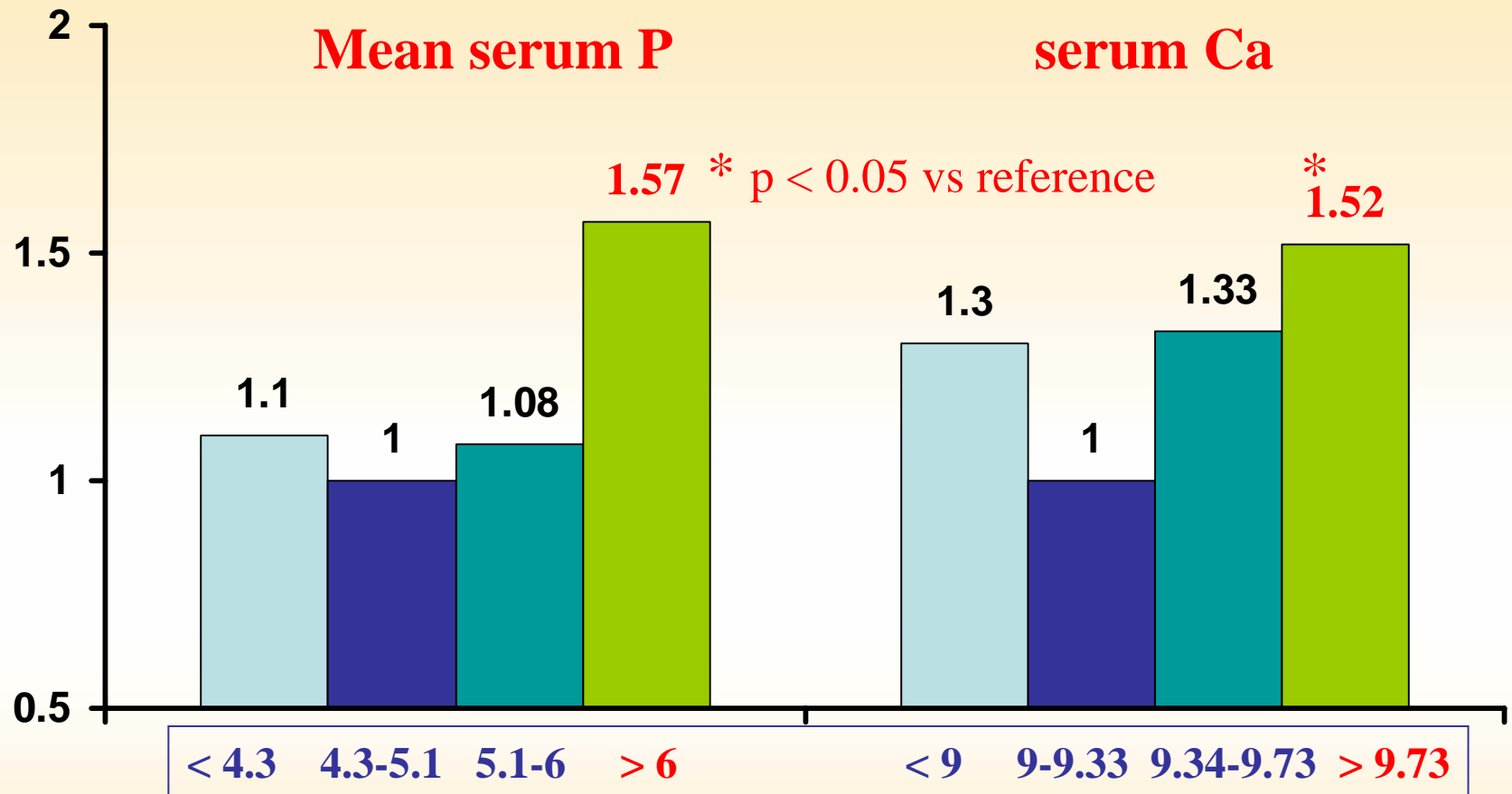
Elevated Serum Phosphorus (> 5) Increases Mortality Risk



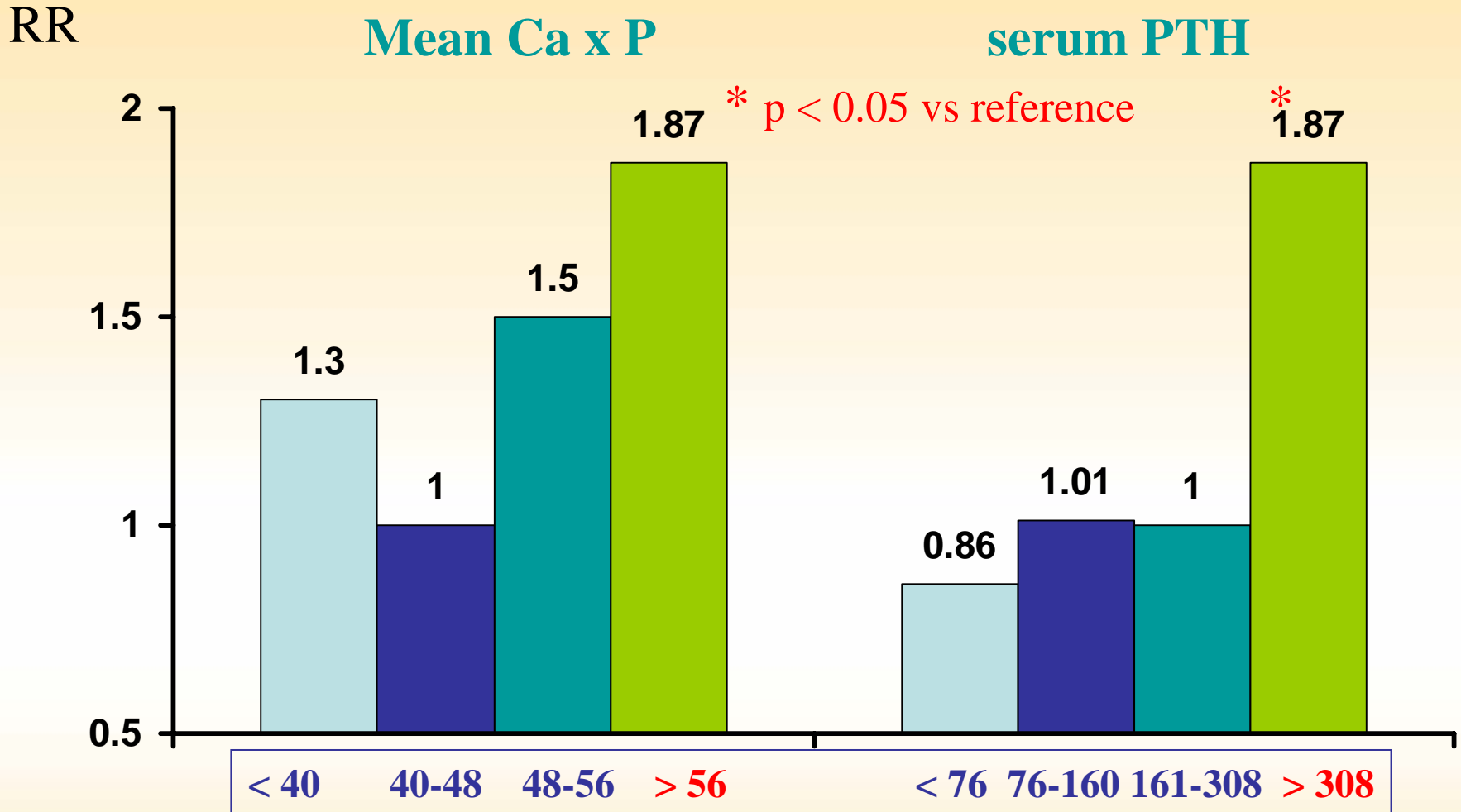
Risk for mortality in 1007 incident dialysis patients (95'-98')

RR

Mean follow up 2.5 yrs

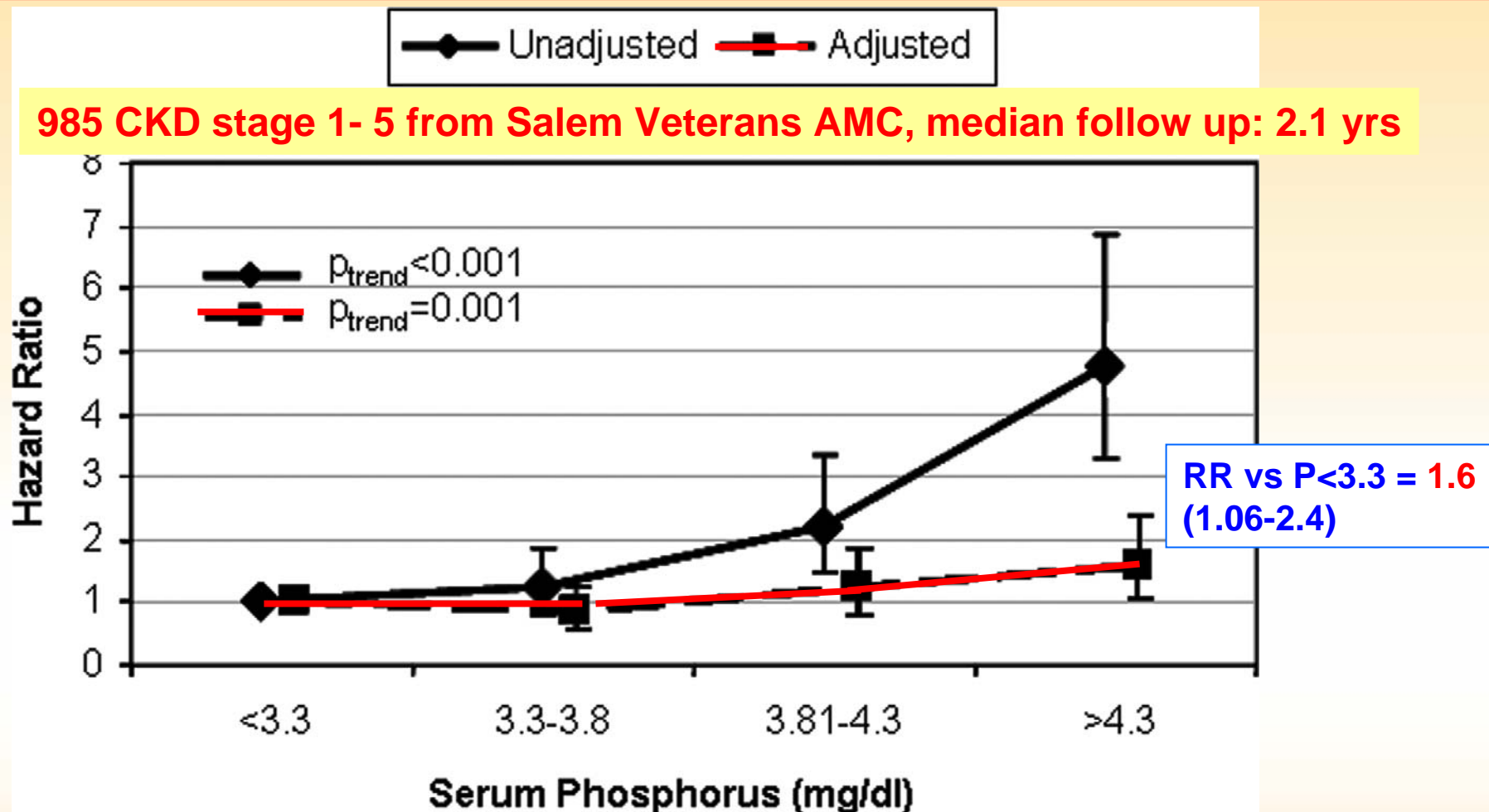


Risk for mortality in 1007 incident dialysis patients (95'-98')



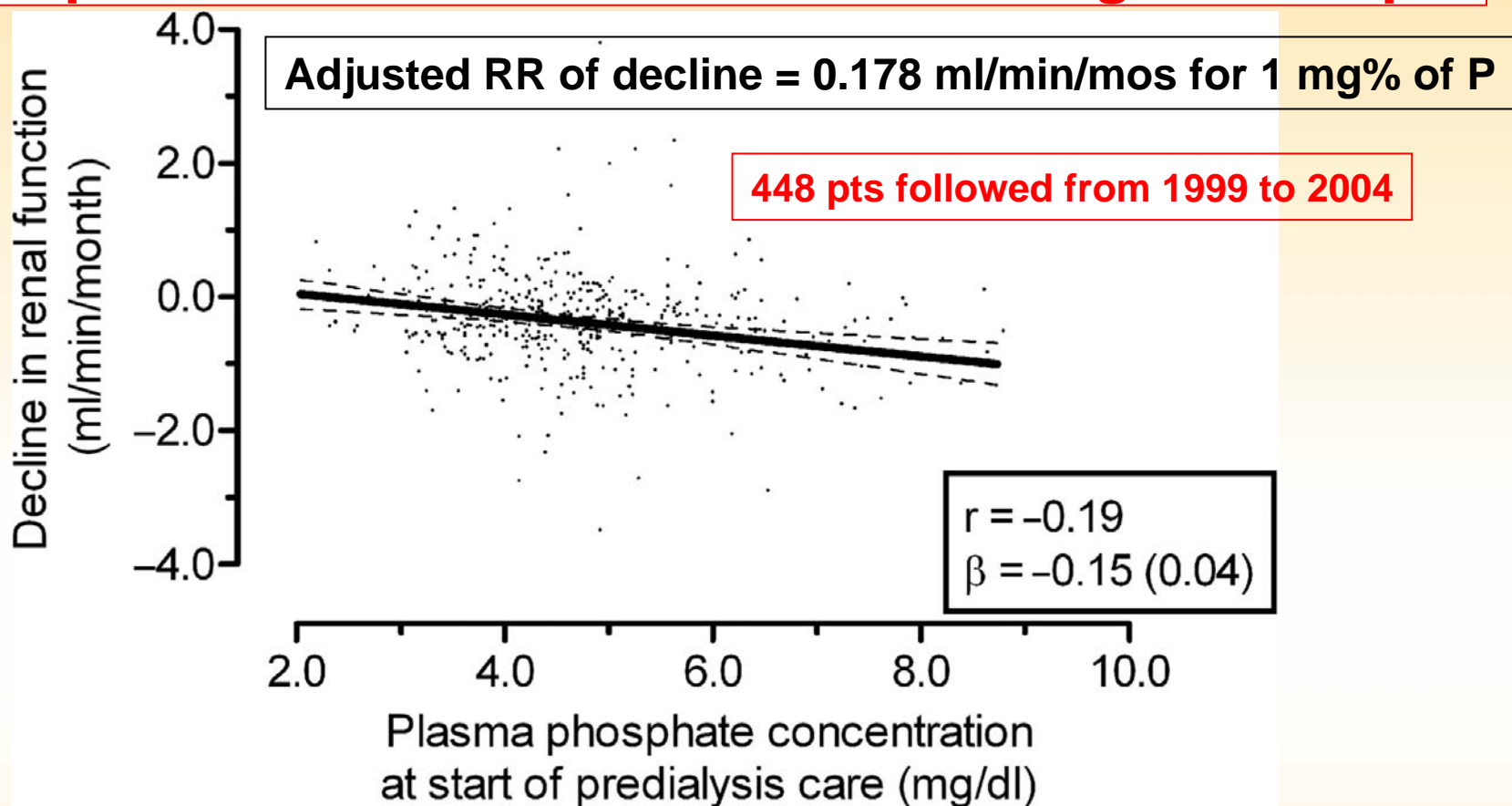
Composite outcome of ESRD and doubling of serum creatinine associated with serum P

unadjusted and **after adjustment** for age, race, systolic (SBP) and diastolic BP (DBP), diabetes, smoking status, estimated GFR (eGFR), serum albumin, calcium, bicarbonate, blood urea nitrogen (BUN), hemoglobin, 24-h urine protein, and use of calcium-containing phosphate binders and angiotensin-converting enzyme inhibitors (ACEI)/angiotensin II receptor blockers (ARB)



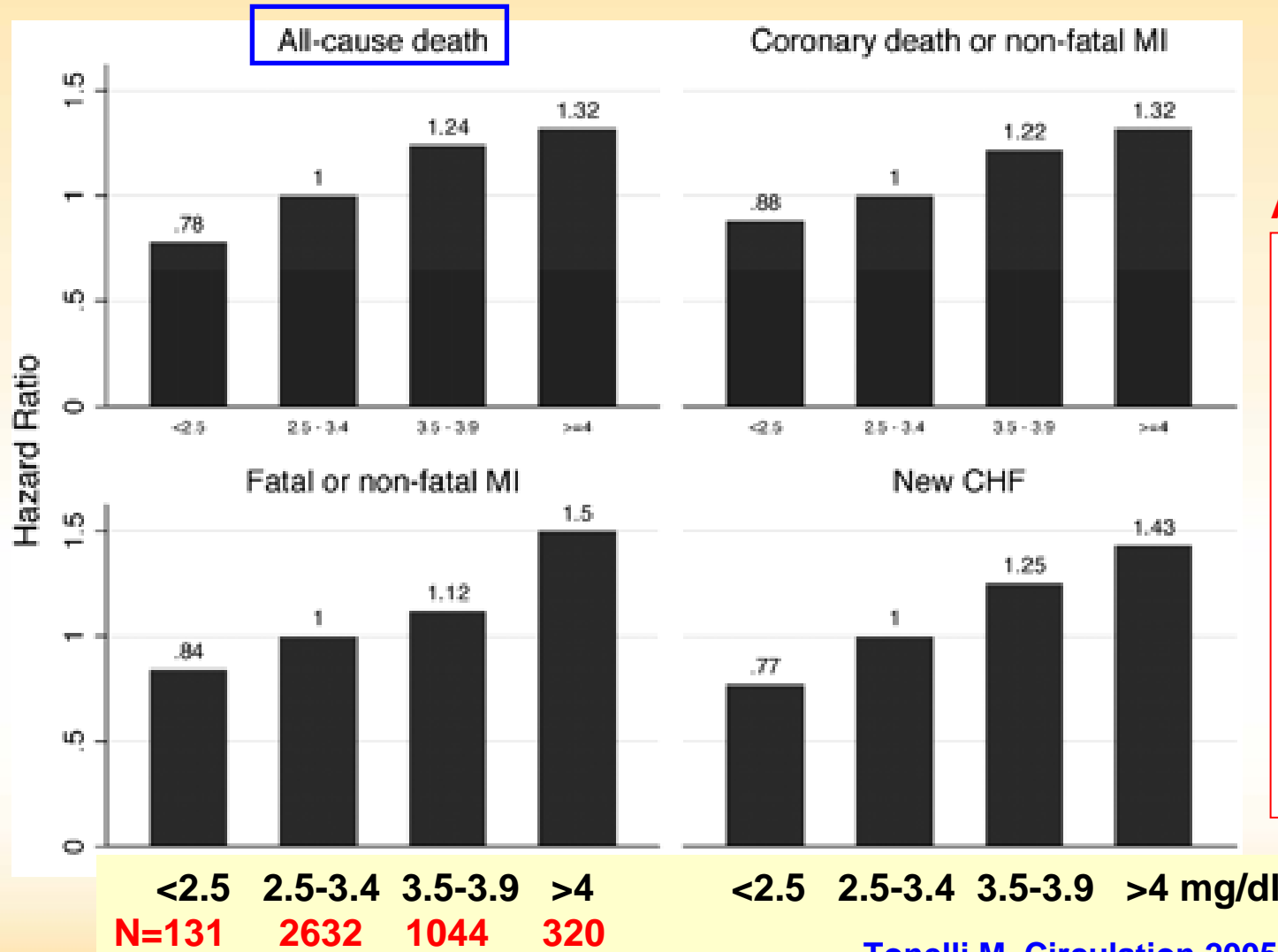
Mortality risk for each mg/dl of P = 1.62
(adjusted for age, sex, GFR, comorbids)

Plasma phosphate at the start of pre-dialysis care and subsequent decline in renal function during follow-up



Baseline P and outcome in 4127 patients with hyperlipidemia and previous MI (CARE study)

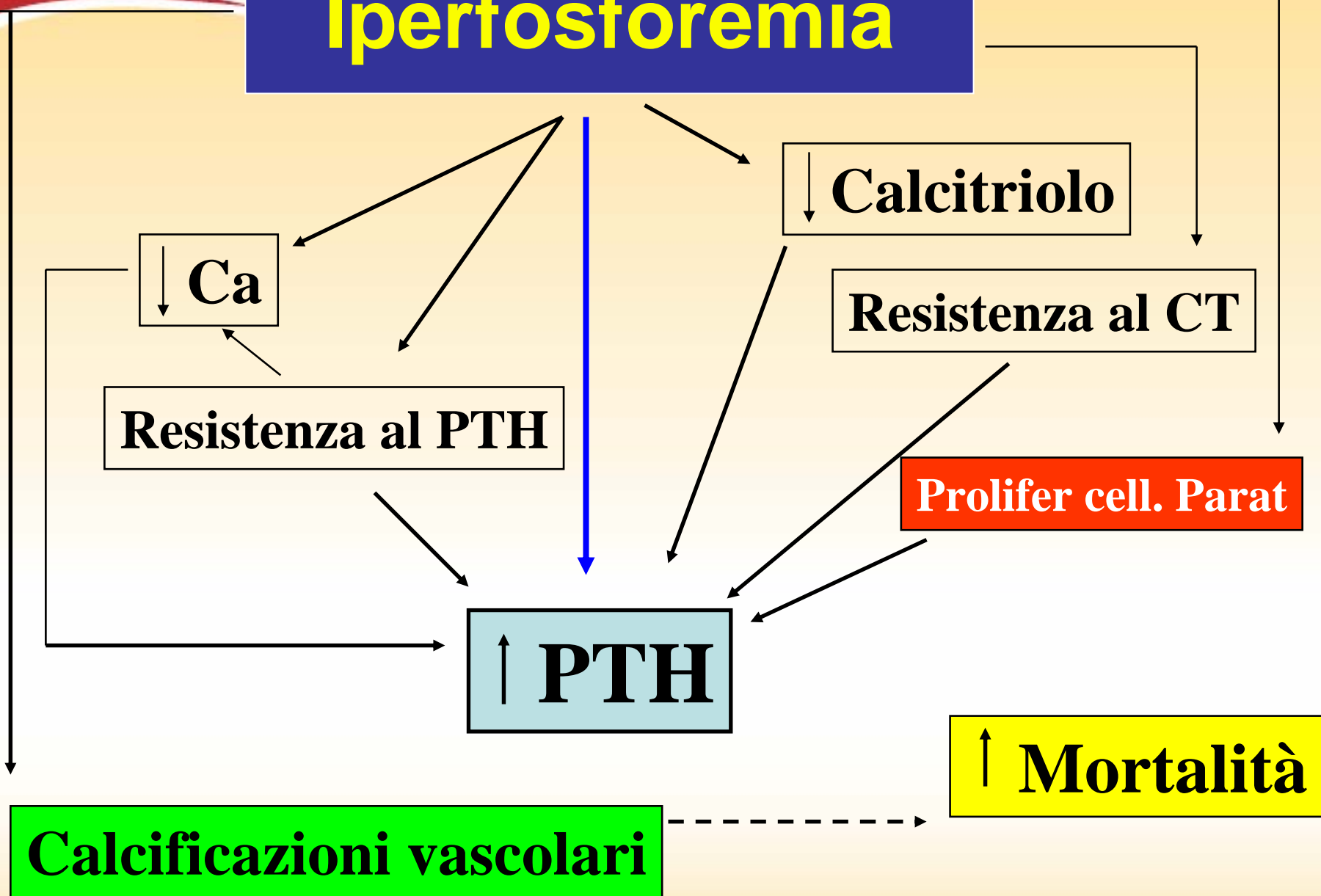
Median follow-up: 60 months, Mean age 58 yrs, Mean GFR = 73 ml/min



Adjusted for

- Age
- Gender
- Race
- Diabetes
- smoke
- glucose
- Albumin
- GFR
- Hb
- FE%

Iperfosforemia



Calcificazioni vascolari

↑ Mortalità

Prolifer cell. Parat

Resistenza al CT

↓ Calcitriolo

Resistenza al PTH

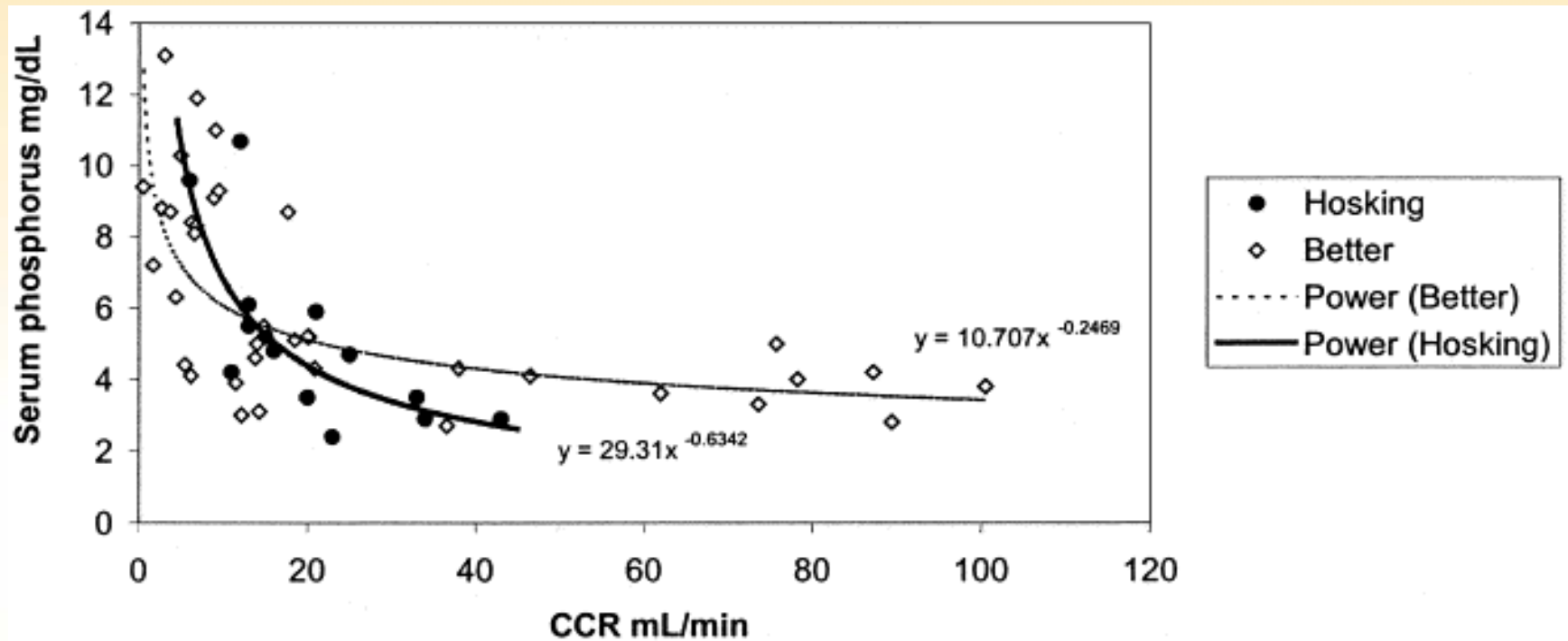
↓ Ca

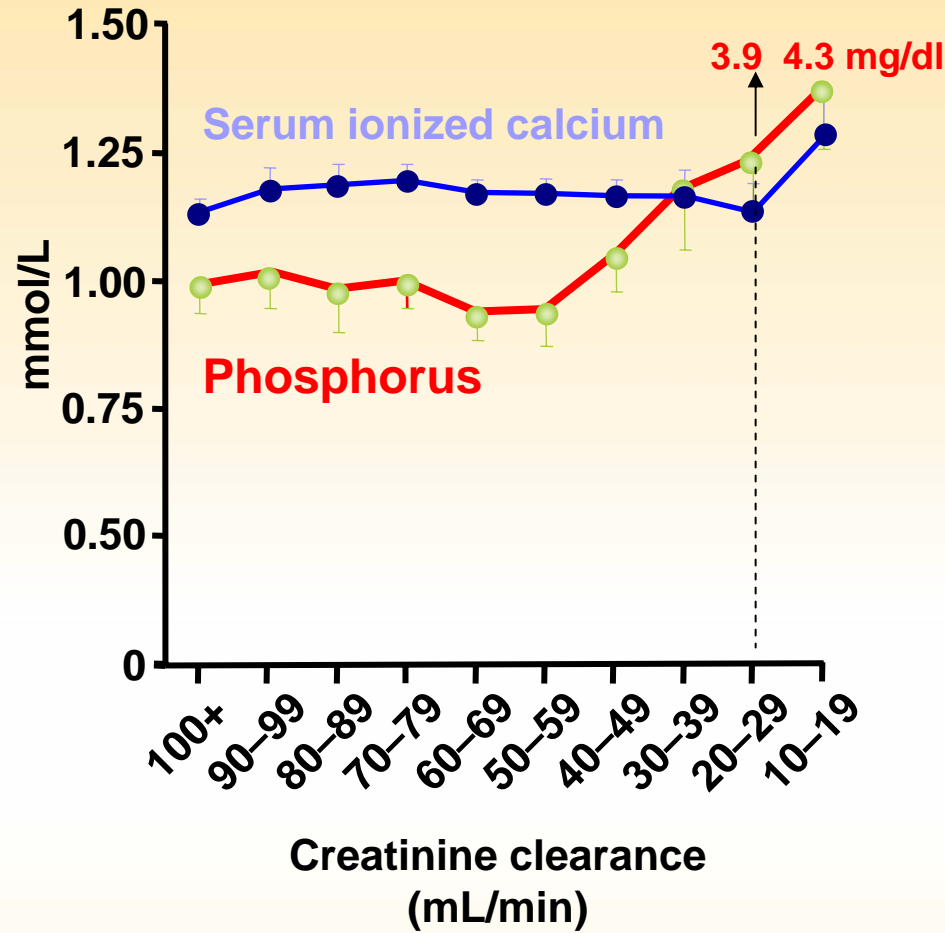
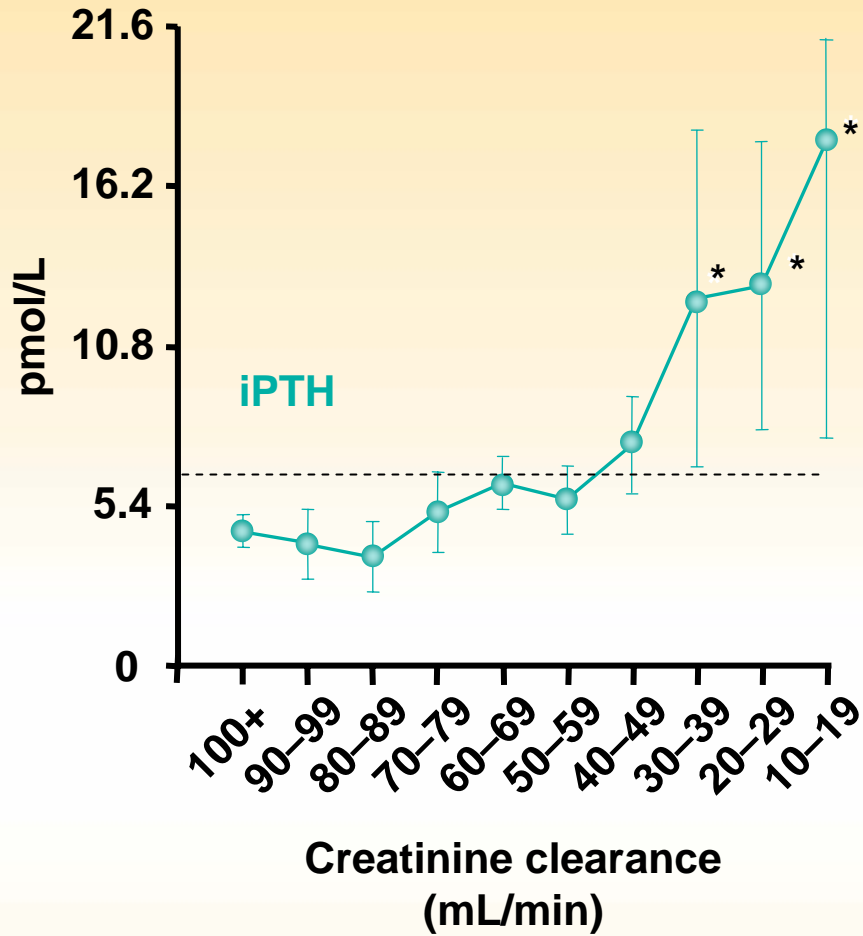
↑ PTH

Eknoyan G *et al.* *Am J Kidney Dis* 2003;42(Suppl 3):1–201

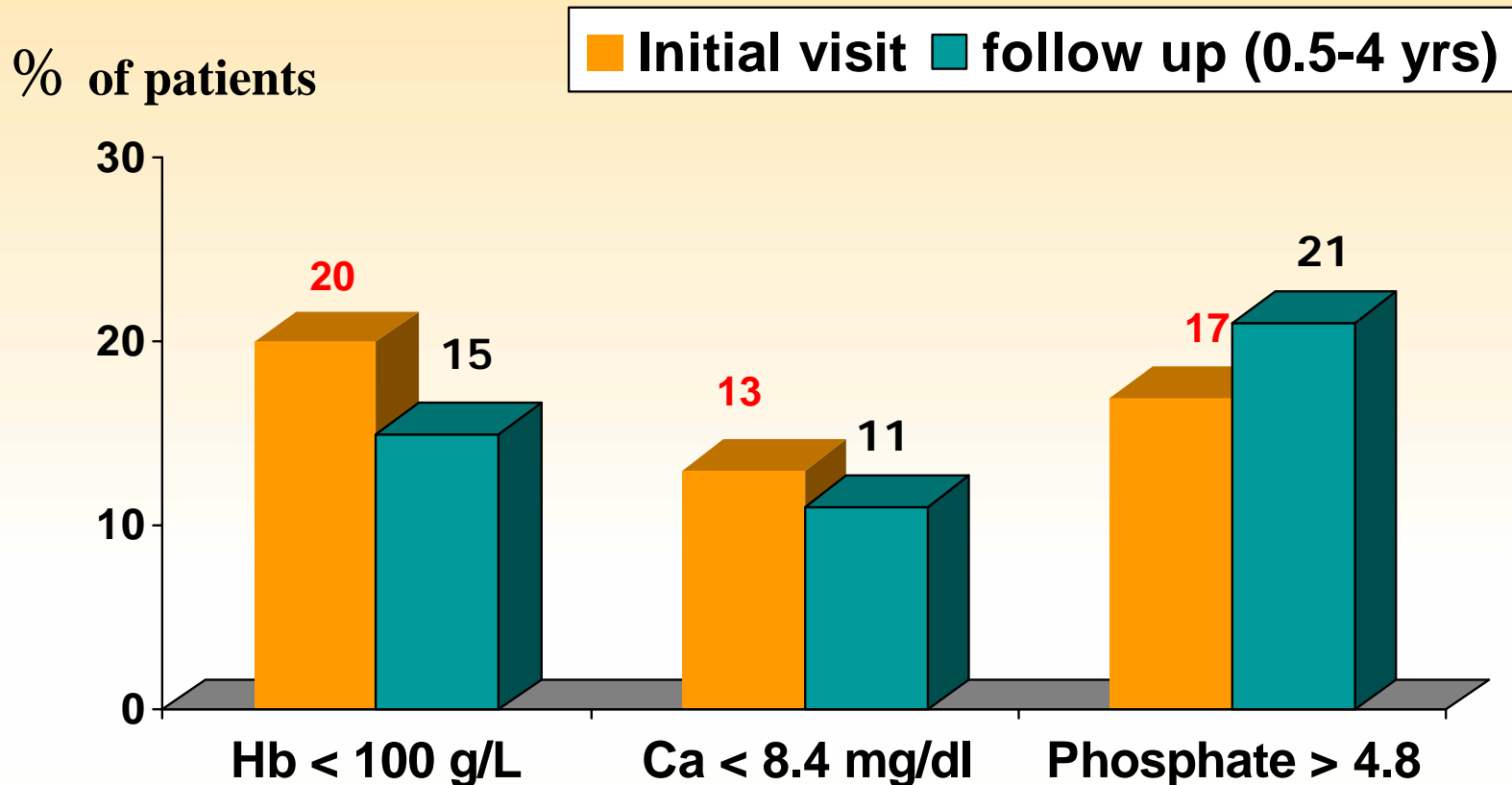
CKD stage	GFR range	PTH target*	P target
3	30-59	35–70 pg/mL [4–8 pmol/L]	2.7–4.6 mg/dl [0.9–1.5 mmol/L]
4	15-29	70–110 pg/mL [8–12 pmol/L]	2.7–4.6 mg/dl [0.9–1.5 mmol/L]
5	< 15	150–300 pg/mL [16.5–33.0]	3.5–5.5 mg/dl [1.1–1.8 mmol/L]
		* Reference = Allegro iPTH Nichols	

Serum P and creatinine clearance

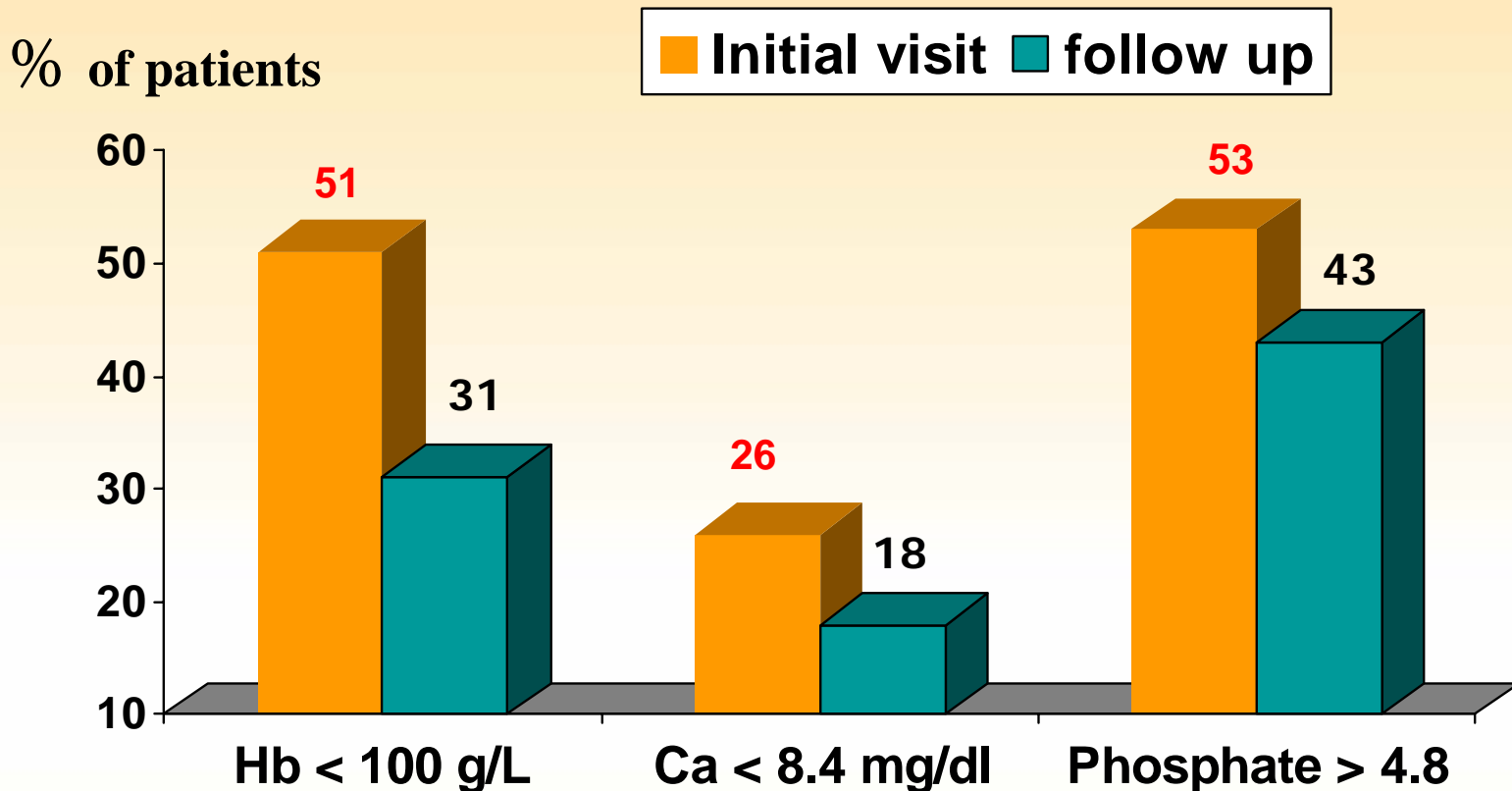




Laboratory data during follow up: 105 CKD (stage 4) patients



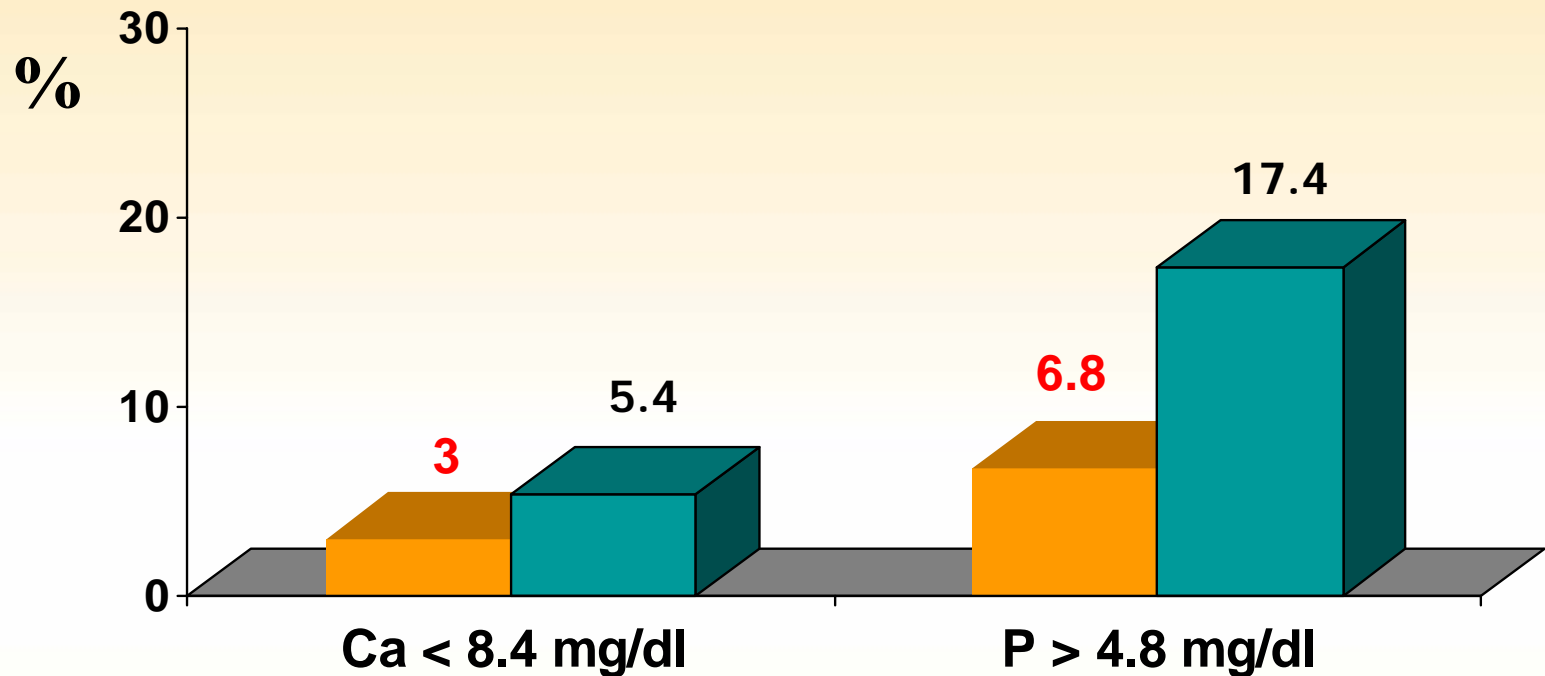
Laboratory data during follow up: 70 CKD (stage 5) patients



Ca and Phosphate levels during follow up: 367 CKD pts followed for at least 3 months

Cremona Hospital (initial visit between 1/01 and 4/05)

■ Initial visit ■ follow up (mean 21, median 18 months)

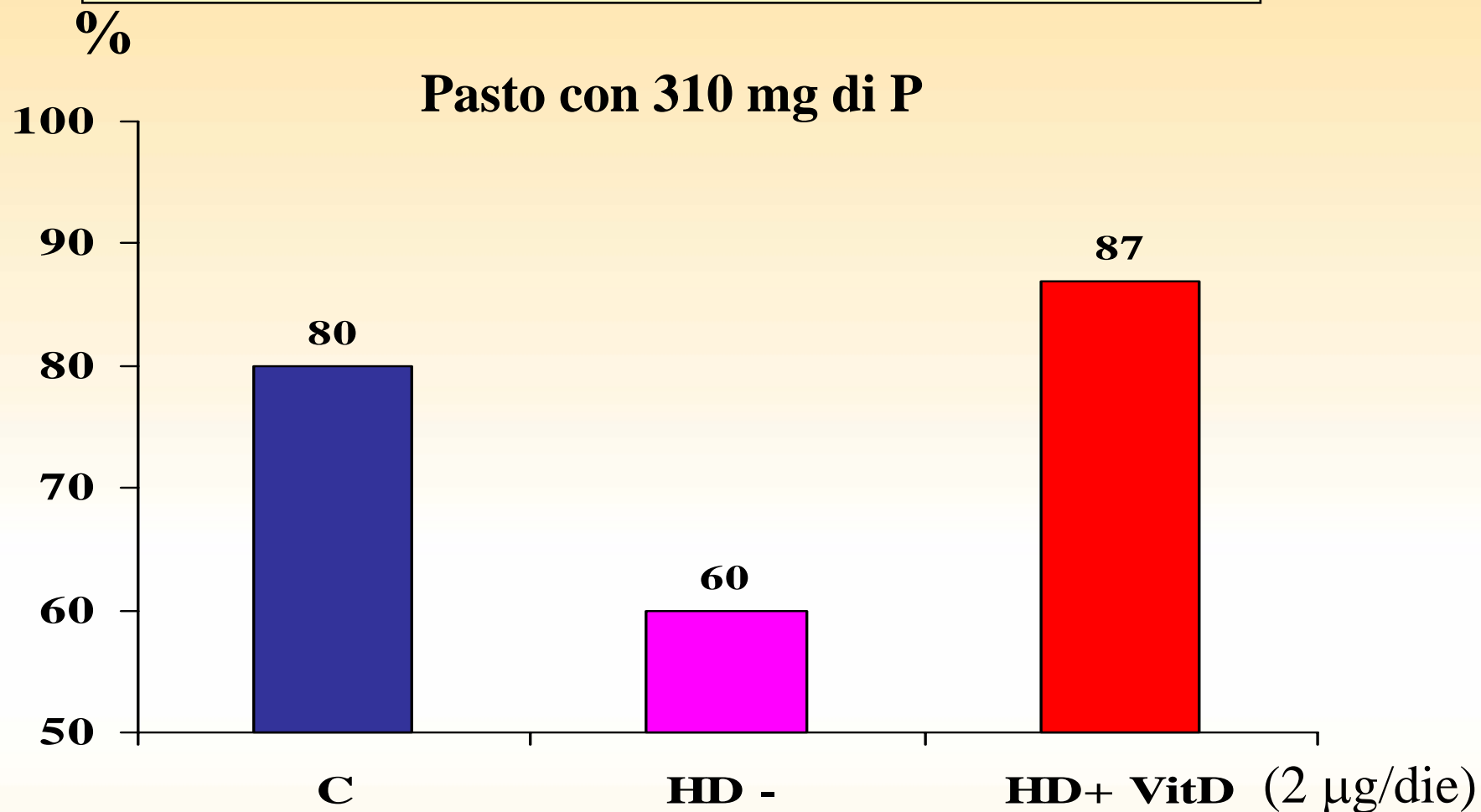


	<u>Initial</u>	<u>last</u>	
GFR (MDRD-6)	28±19	25±19	ml/min/1.73m ² (p < 0.001 vs initial)
Stage V, % of pts	19	33	

Fattori che influenzano la FOSFOREMIA

- **Apporto dietetico di P**
- **Assorbimento intestinale:**
 - Terapia con chelanti del Fosforo
 - Terapia con metaboliti della vit. D
- **Compliance**
- **Terapia con chelanti**
- **Efficienza dialitica**
- **Iperparatiroidismo severo**
- **Ipercatabolismo**
- **Farmaci o prodotti contenenti P (lassativi, ecc.)**

Assorbimento intestinale di P



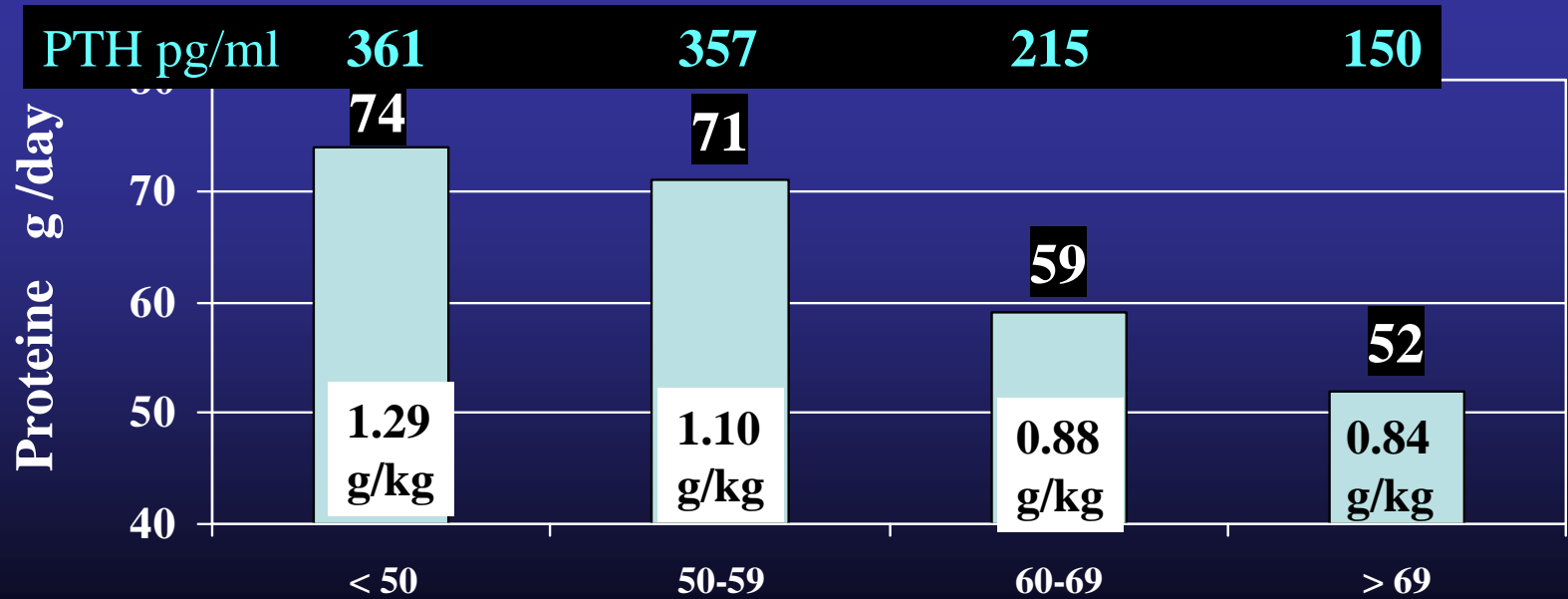
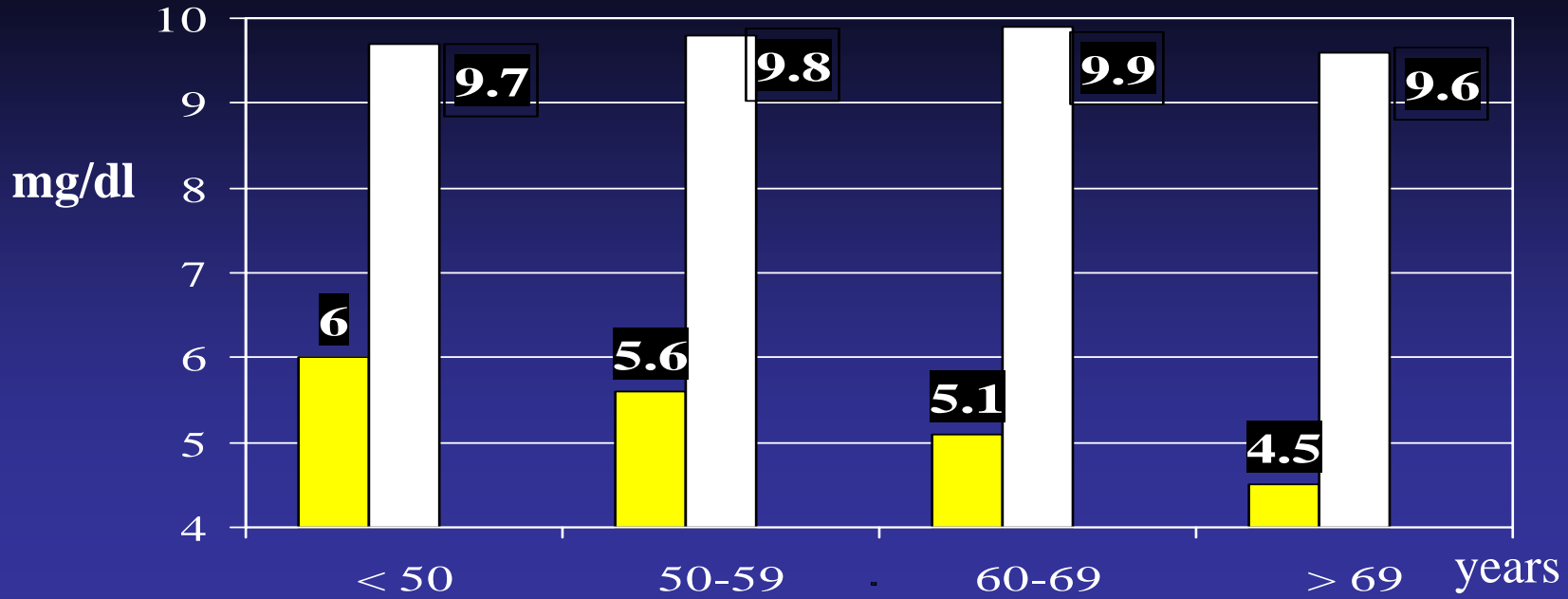
Ramirez KI 1986; 30: 753

Dietary P Content by Protein Intake in 60 Heart Disease Patients

Protein intake (g/kg/day)	Dietary P (mg)
>1.2	1353 ± 253
1.0-1.2	1052 ± 219
0.8-1.0	936 ± 217
0.6-0.8	831 ± 142
<0.6	599 ± 105

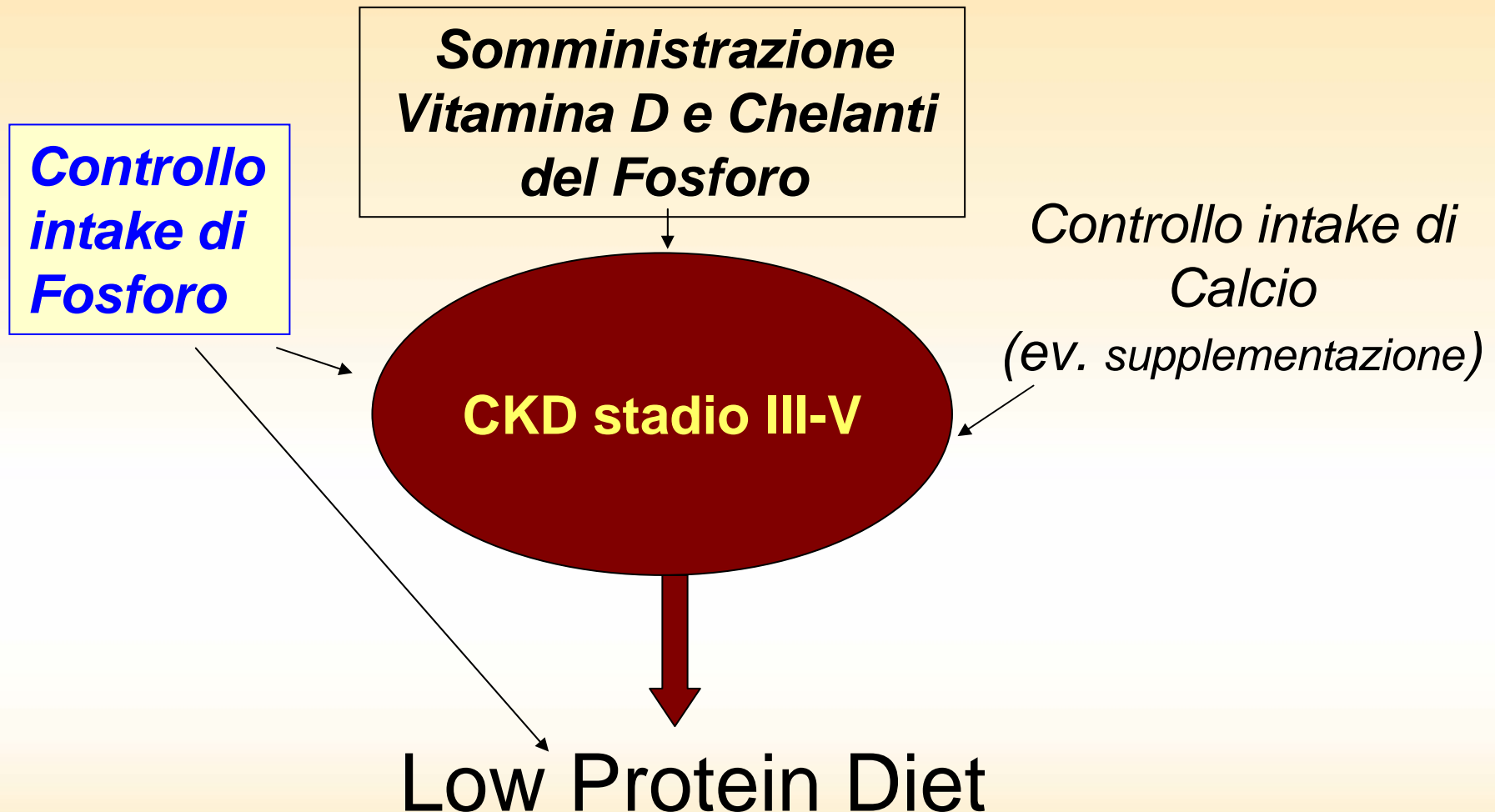
N° = 207 dialysis pts

■ P □ Ca



Lorenzo V et al AJKD 2001, 37: 1260-6

Strategie terapeutiche nel paziente con CKD



Control of secondary HPT during 4 yrs follow up of protein-restricted diet

Dietary regimen: 40 Kcal/kg, 0.6 g/Kg of protein, 600-700 mg of P

creatinine mg/dl

3.10
± 0.20

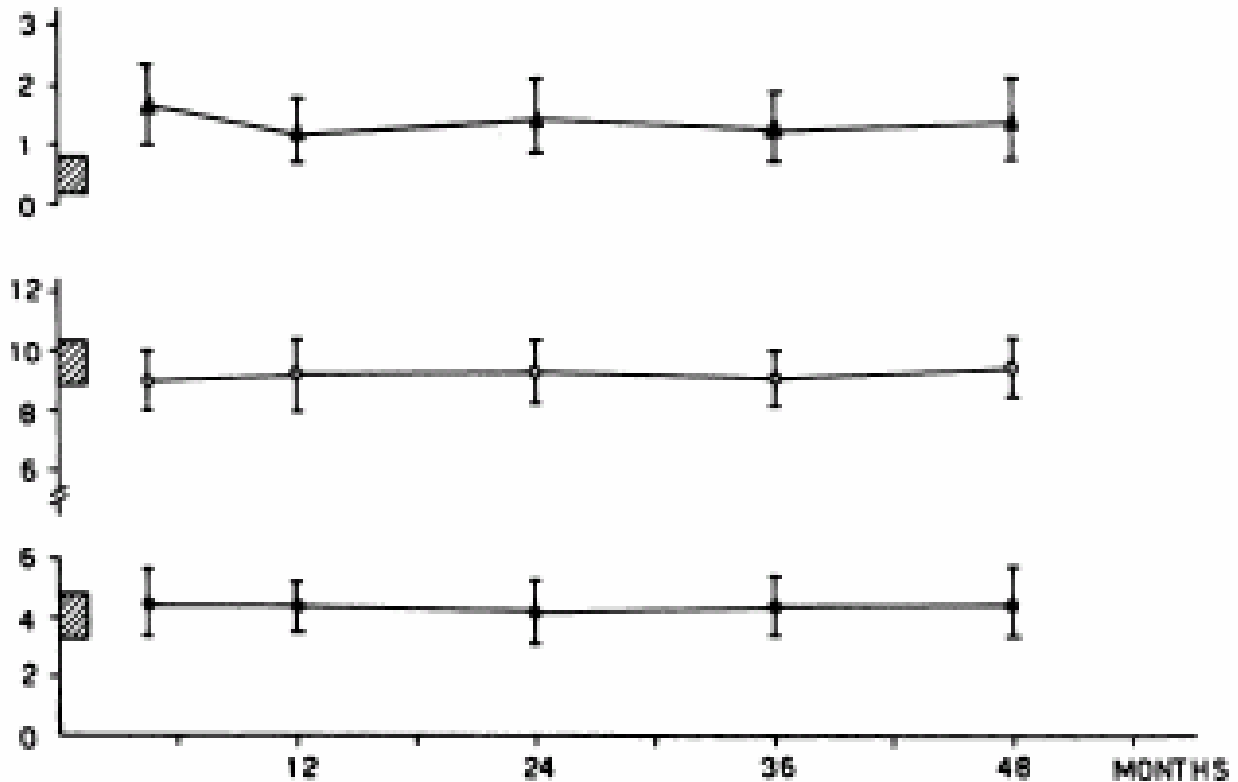
3.48
± 0.90

4.20
± 1.00

5.40
± 2.05

6.35
± 1.85

PLASMA i-PTH
µg/l

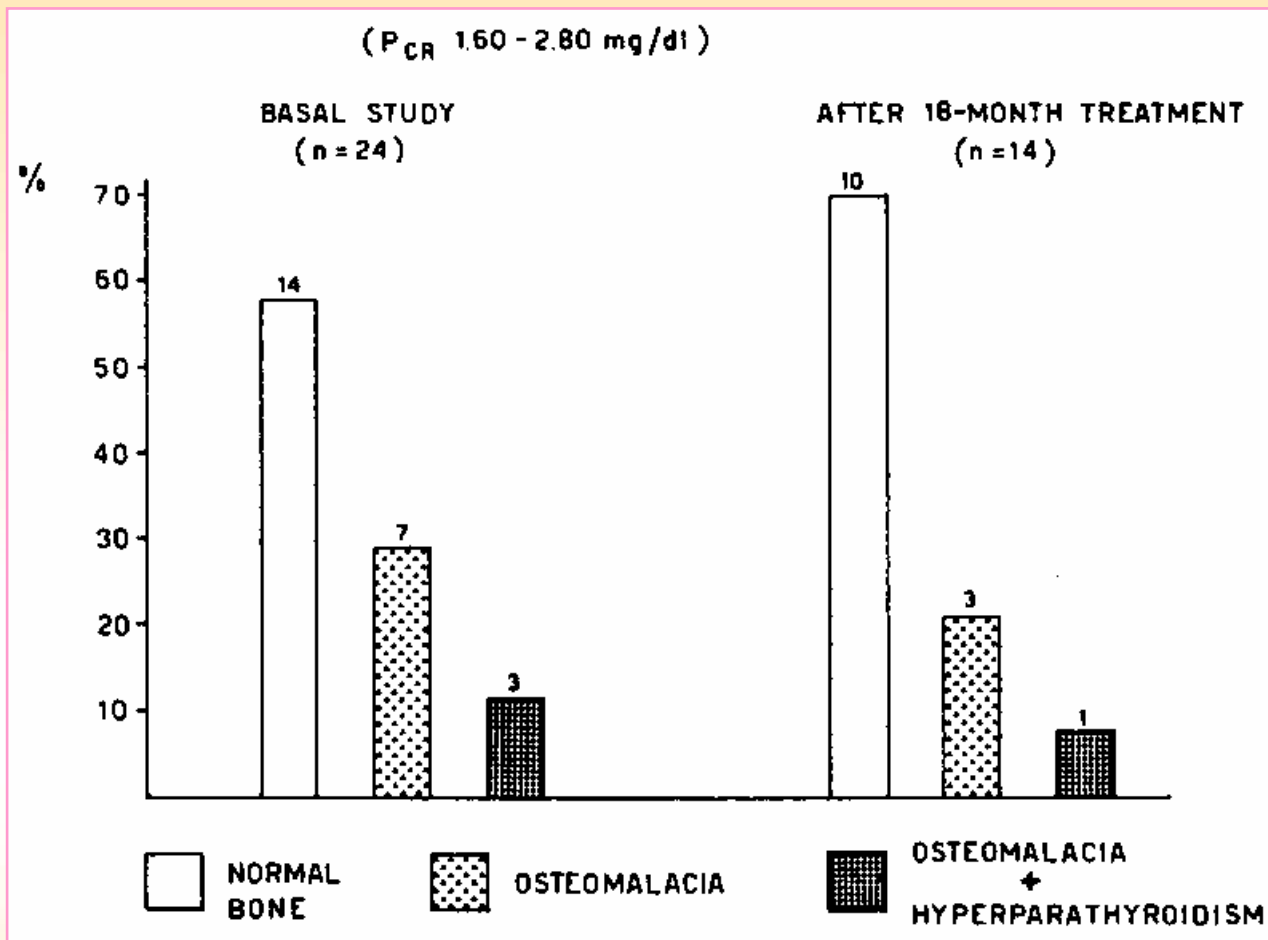


N = 36

(Intermittent Vit D3
Ca++ supplements)

■ NORMAL RANGE

Dieta Ipoproteica ed IperPTH

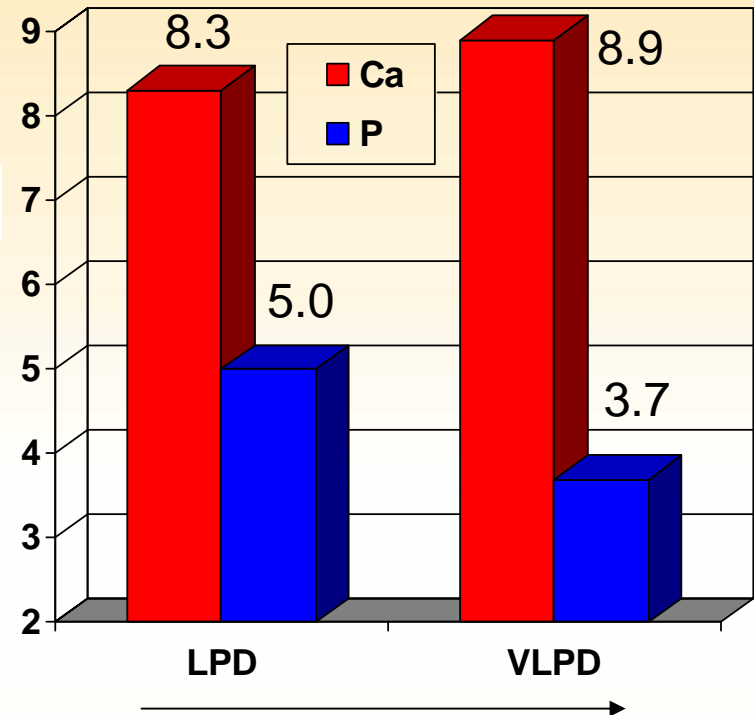
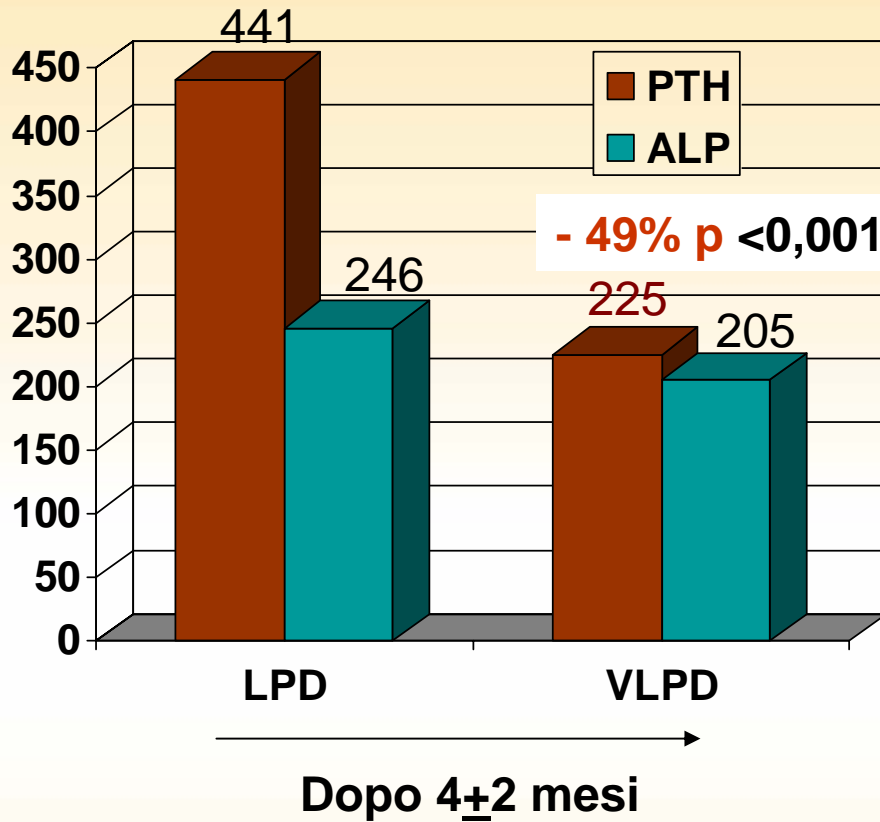


Dopo 18 mesi di trattamento LPD nei pazienti con IRC (cr. 1,6-2,8 mg/dl), si osservava un miglioramento delle patologie a ridotto ed elevato turn-over.

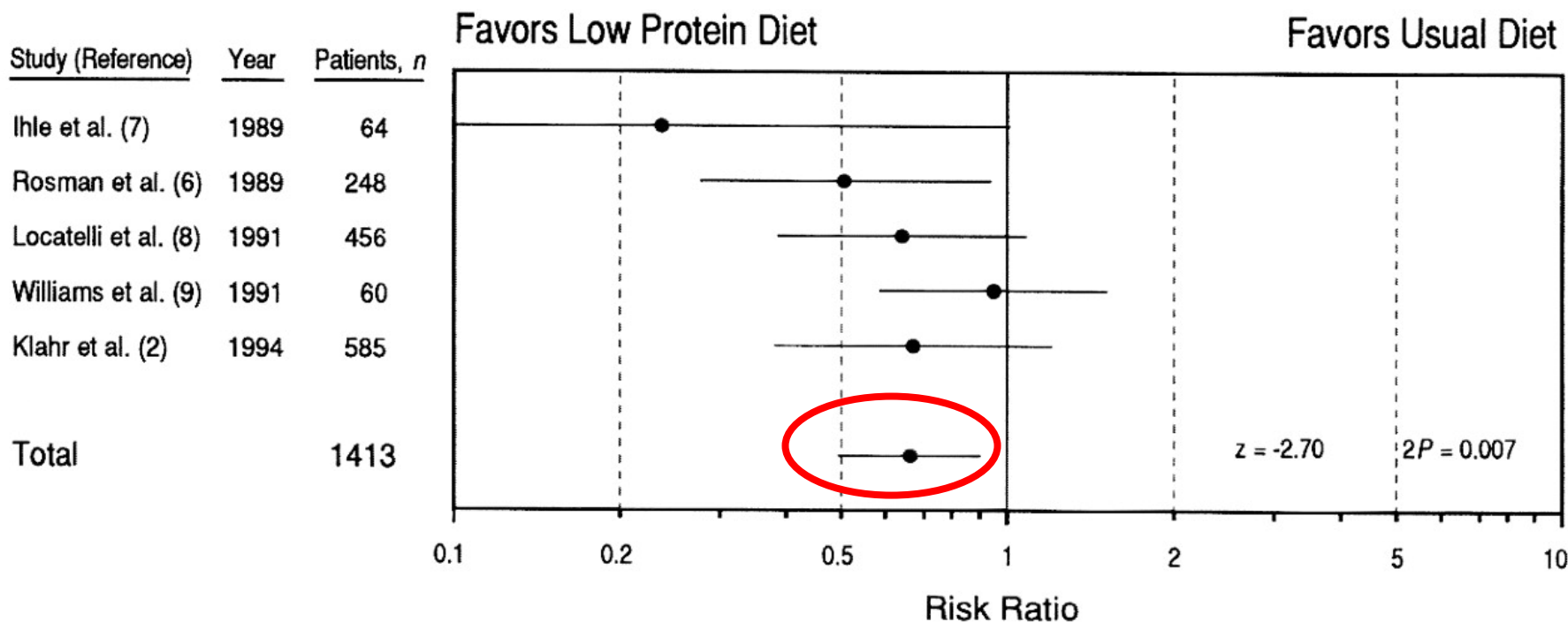
Dieta Ipoproteica ed IperPTH

- 21 Pazienti con **CKD (stadio V, Creatinina > 6.5) e PTH >150 pg/ml**
- **EFFETTO** della restrizione dietetica di P
- **BASALE** dieta da basso contenuto di proteine (**0,6 g/kg**) ---> **VLPD** (**0,3 g/kg, P 5 mg/Kg**), supplementate con chetoanaloghi, calcio-carbonato (2-4 g/die) e vitamina B12. Entrambi i regimi dietetici avevano lo stesso contenuto calorico (**35 Kcal/kg**).

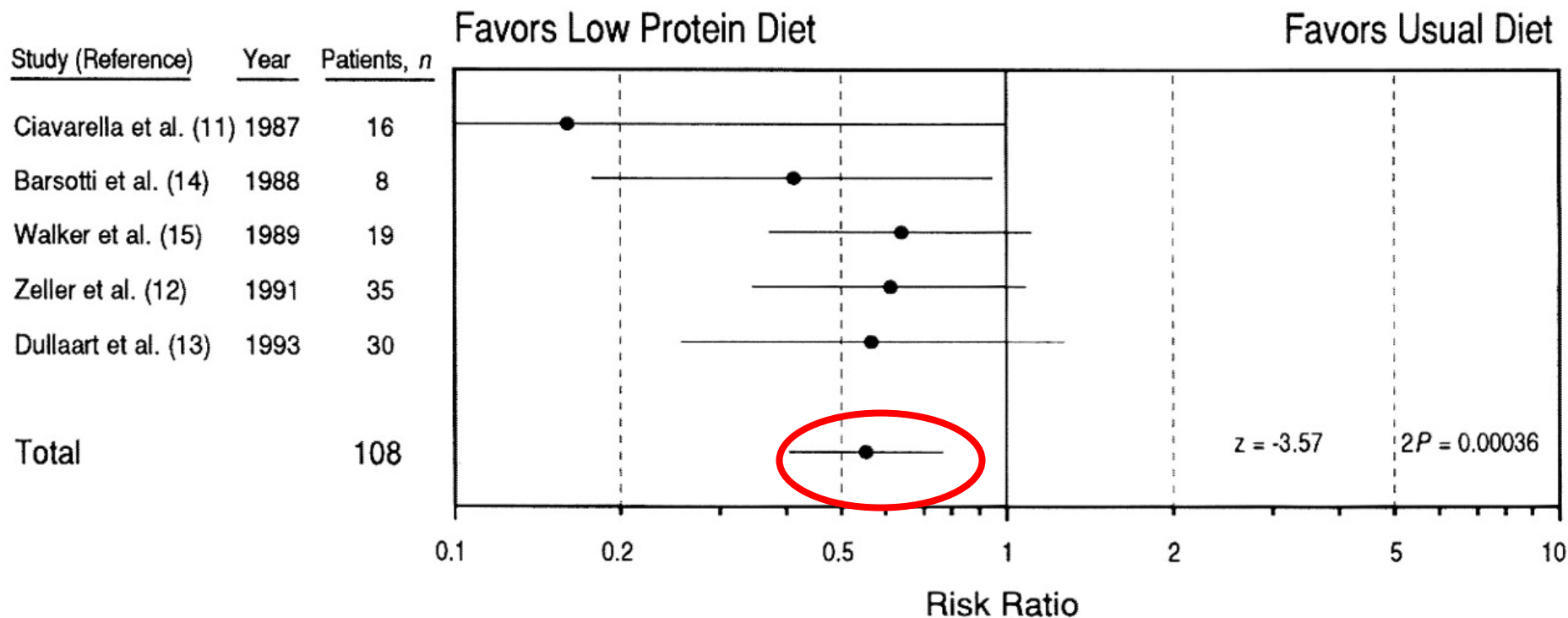
Dieta Ipoproteica ed IperPTH



Effect of dietary protein restriction on progression of nondiabetic renal diseases

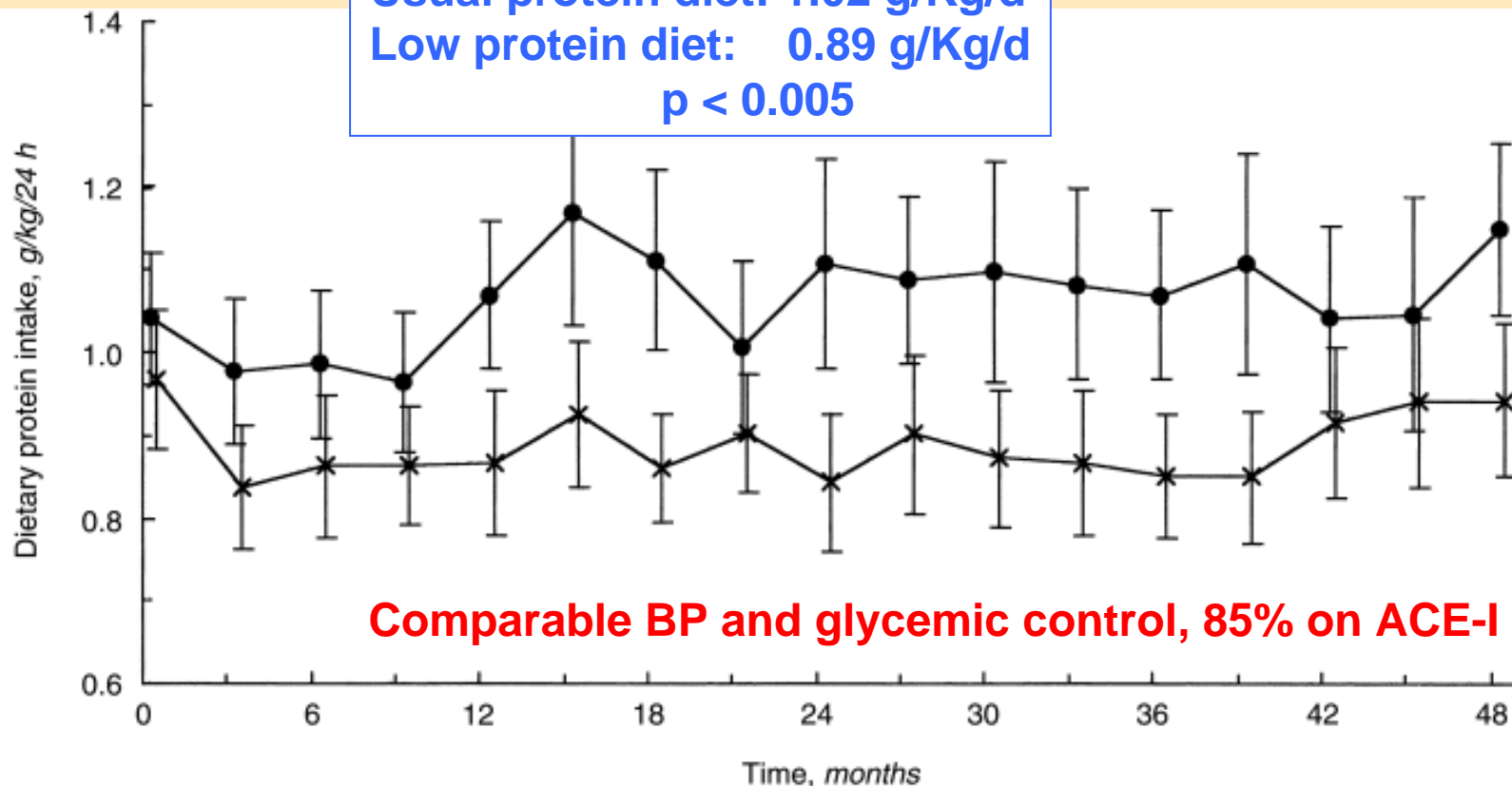


Effect of dietary protein restriction on progression of diabetic renal disease



Estimated dietary protein intake in type 1 diabetic patients with progressive nephropathy (mean GFR decrease: 7.1 ml/min/yr).

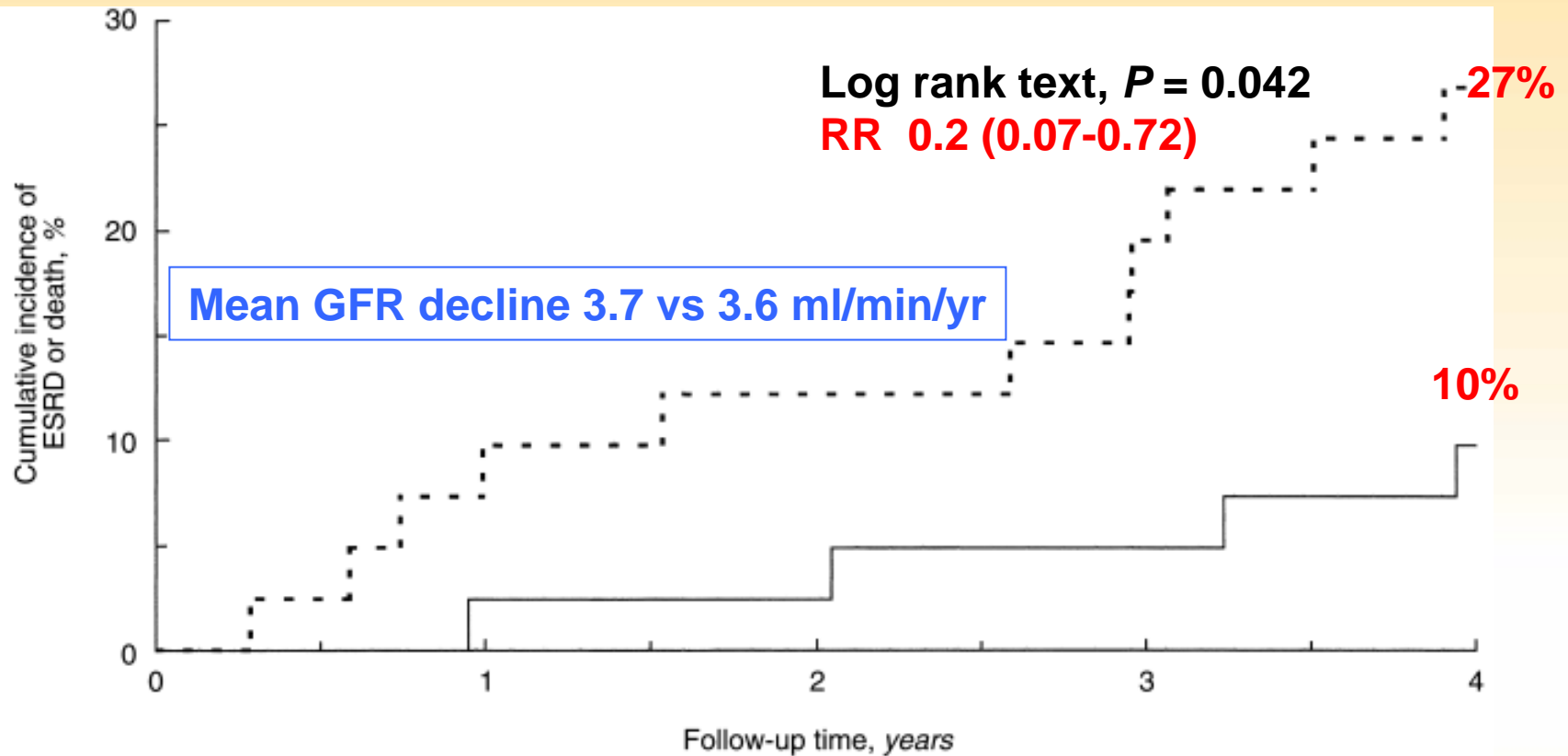
Usual protein diet: 1.02 g/Kg/d
Low protein diet: 0.89 g/Kg/d
 $p < 0.005$



Comparable BP and glycemic control, 85% on ACE-I

Usual-protein diet	41	38	36	34	34	33	32	27	30	30	30	28	27	24	27	24	27
Low-protein diet	41	39	38	35	38	35	37	35	36	35	36	34	36	31	34	37	36

Cumulative incidence of ESRD or death in type 1 diabetic pts with diabetic N in the usual-protein group (dashed lines) and the low-protein diet group.



Usual-protein diet	41	40	37	37	36	36	33	31	30
Low-protein diet	41	41	40	40	40	39	39	38	37

K/DOQI Recommendations on dietary P restriction (Guideline 4 & 5, AJKD 2003):

- **Dietary P restricted to 0.8-1 g/day when:**
 - Serum P > 4.6 - Stage III-IV (**opinion**)
 - Serum P > 5.5 - Stage V (**evidence**)
 - PTH levels are increased (**evidence**)
- **If serum P cannot be controlled by dietary restriction (**Stage III and IV**):**
 - P binders should be prescribed (**opinion**)
 - Ca salts are effective in lowering serum P (**evidence**) and may be used as the initial binder therapy (**opinion**)

K/DOQI Recommendations on dietary protein restriction in diabetics (AJKD 2007, S2: S95-S107):

- **0.8 g/Kg/BW/day in CKD I-IV: :**
 - Reduce albuminuria and progression of renal insufficiency
- **Protein intake < 20% of total daily calories**



Nephrontieres

Focus on Diet in Nephrology



Nephrontieres

Focus on Diet in Nephrology

Fosforo e Dieta Ipoproteica

Il fosforo è un costituente chiave delle **proteine** di origine animale.

1 g di proteine = circa 13 mg di fosforo

Apporto di fosforo consigliato:

circa 800 mg/die

In un soggetto di 70 kg:

Una dieta di 1,2 g prot/kg: Fosforo \pm 1.100 mg

Una dieta di 0,6-0,8 g prot/kg: Fosforo \pm 800 mg

Fosforo = consigli dietetici

Un metodo per ridurre ulteriormente il contenuto dei fosfati con la dieta è quello della bollitura.



Il 21-27% di fosforo può essere eliminato dai cibi vegetali come anche da quelli animali.

Restrizione fosforica nella IRC

- **Dieta ipoproteica ipofosforica**

Proteine: 0.6 g/kg/die **Fosforo:** 7-8 mg/Kg/die

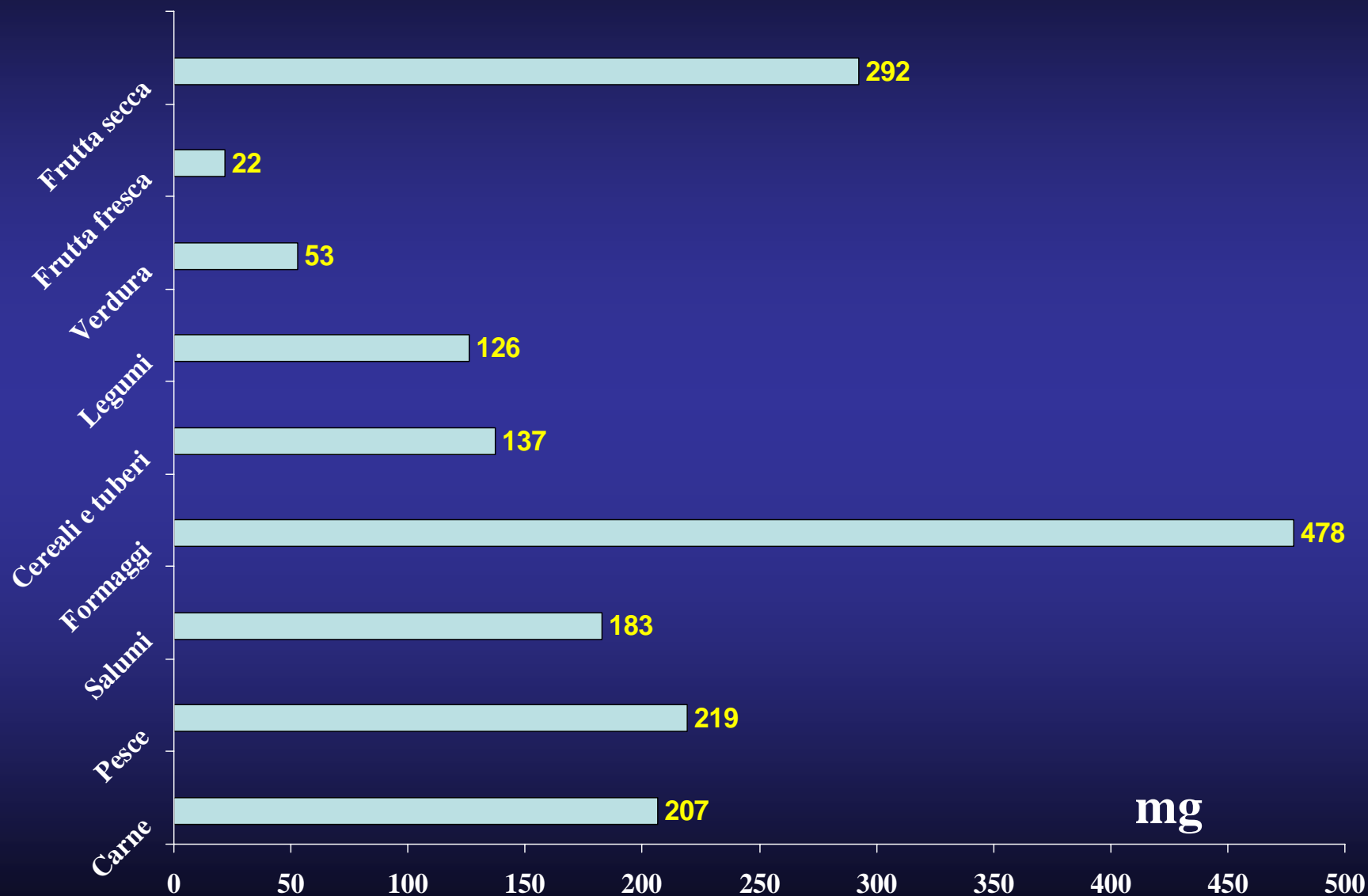
Supplementazione Calcio carbonato

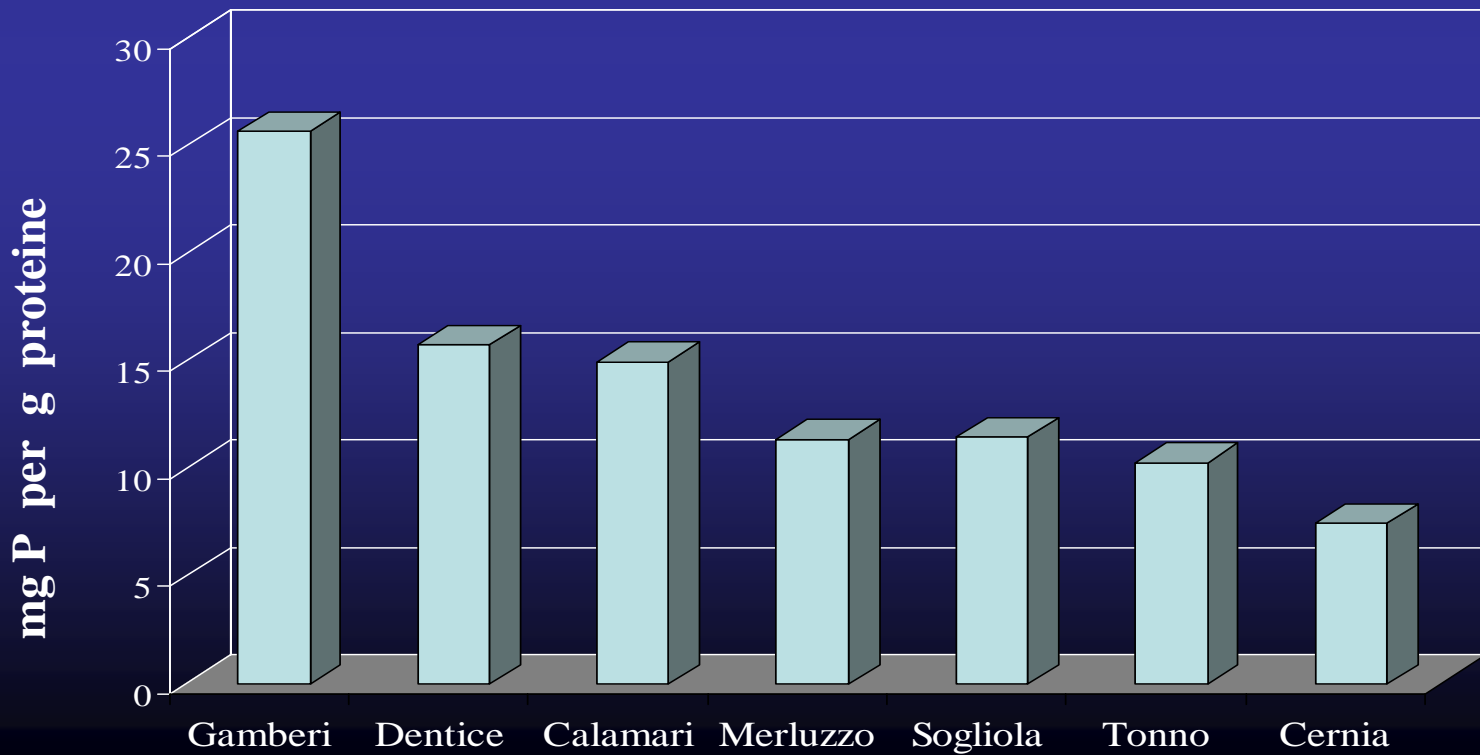
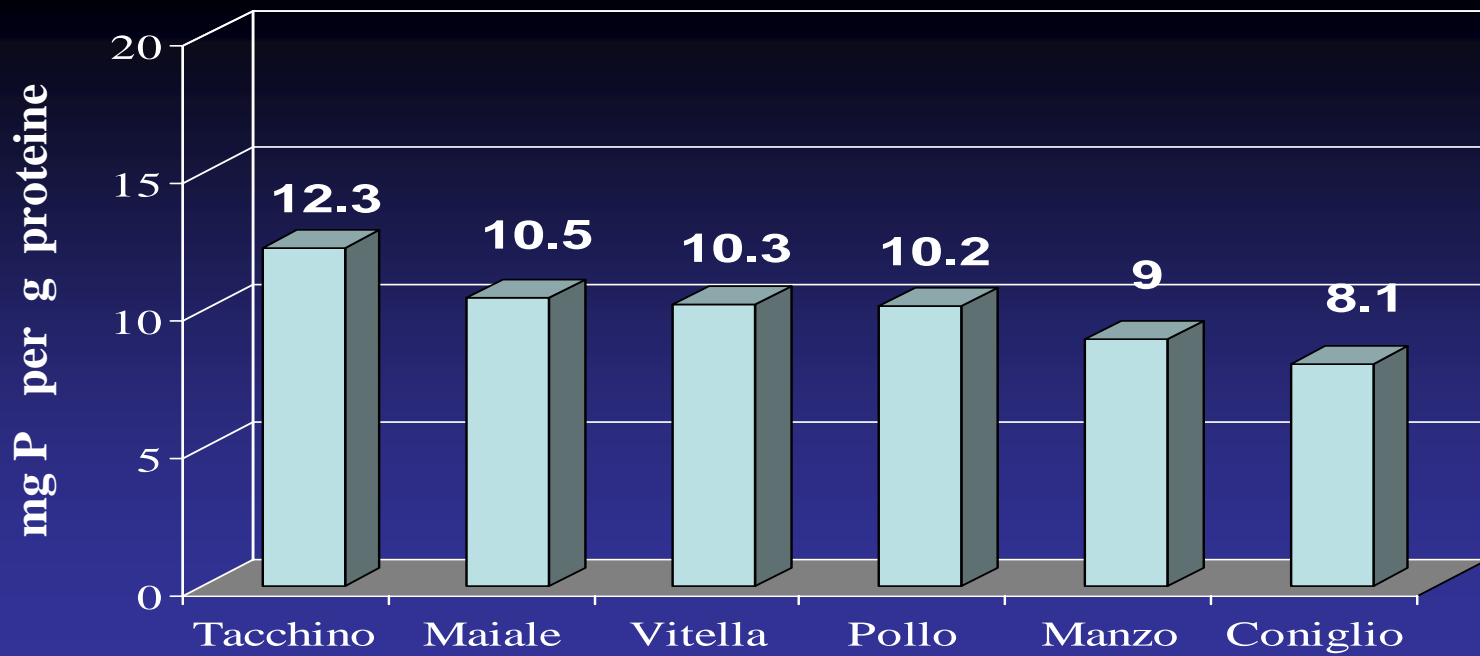
- **Dieta fortemente ipoproteica ipofosforica supplementata con AA essenziali e chetoacidi**

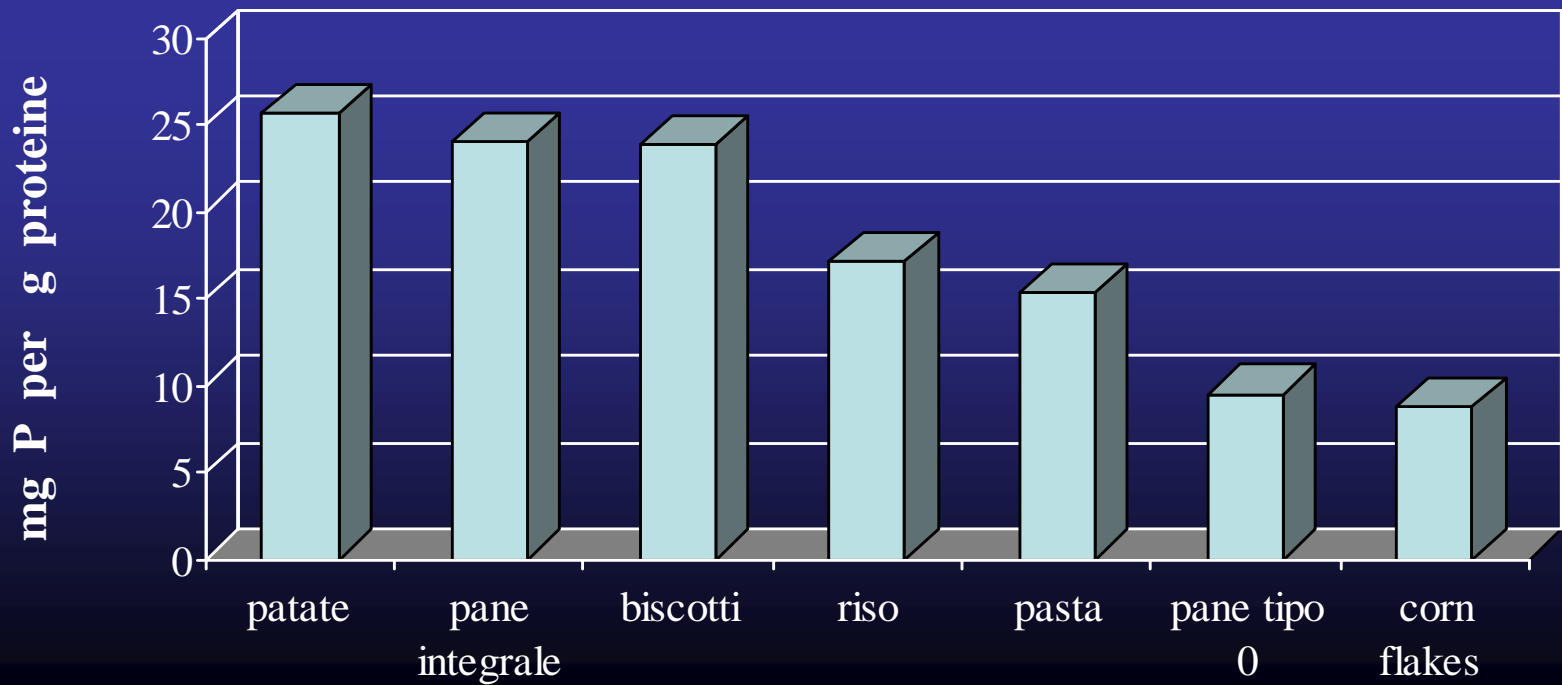
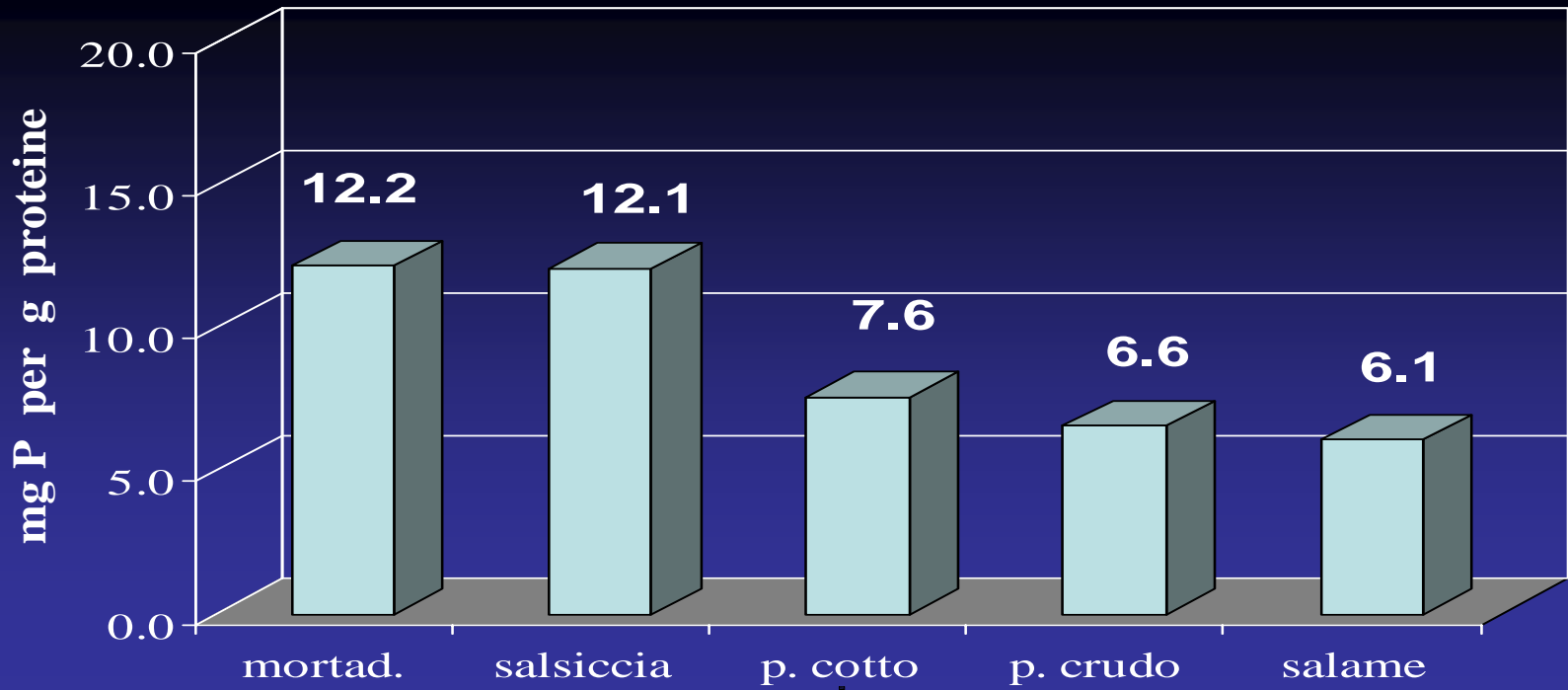
Proteine: 0.3 g/kg/die **Fosforo:** 3-5 mg/Kg/die

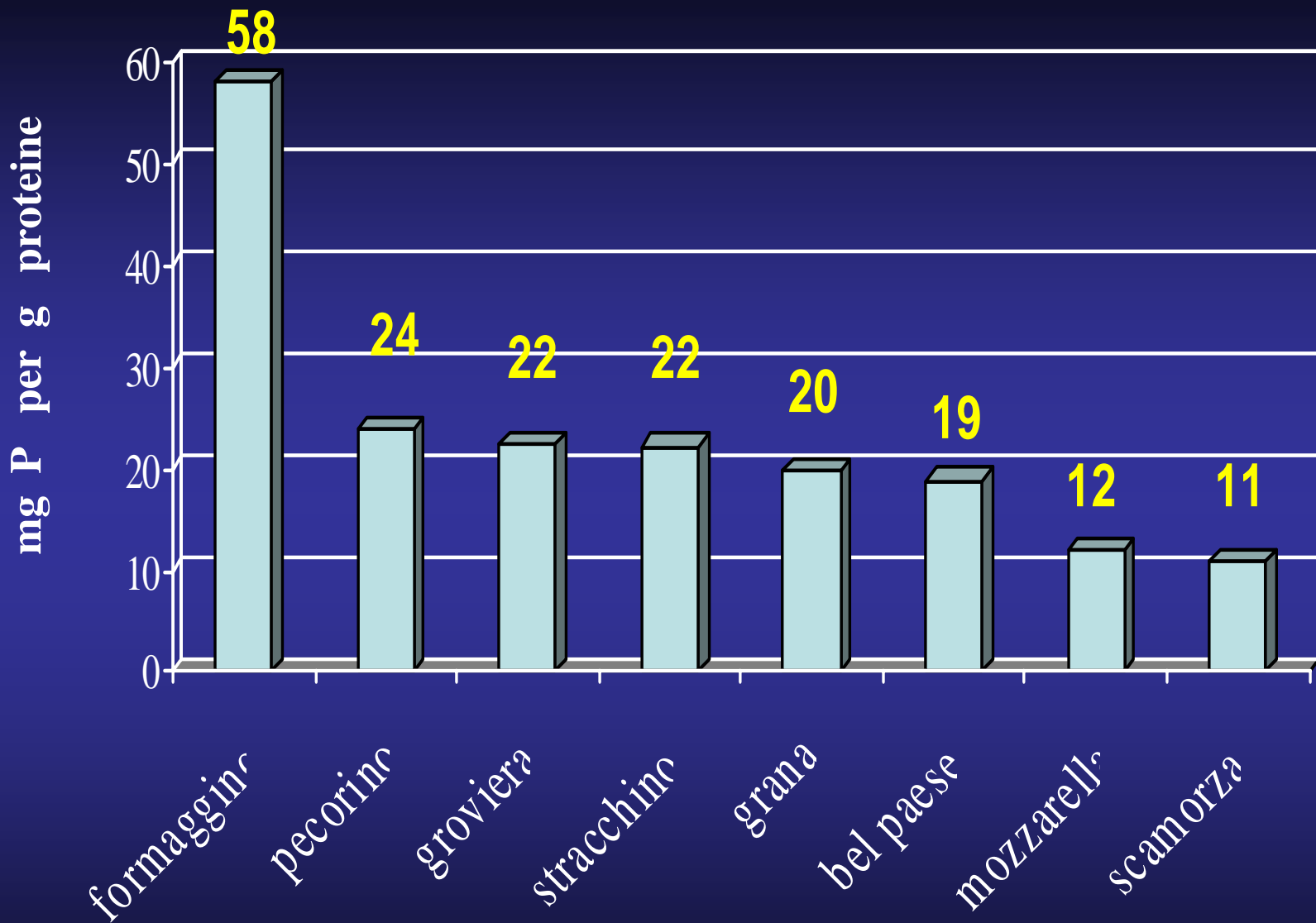
Supplementazione AA essenziali e chetoacidi: 0.1 g Kg
Calcio carbonato, Vitamina B12,ferro

Contenuto medio di Fosforo per 100 g di alimento

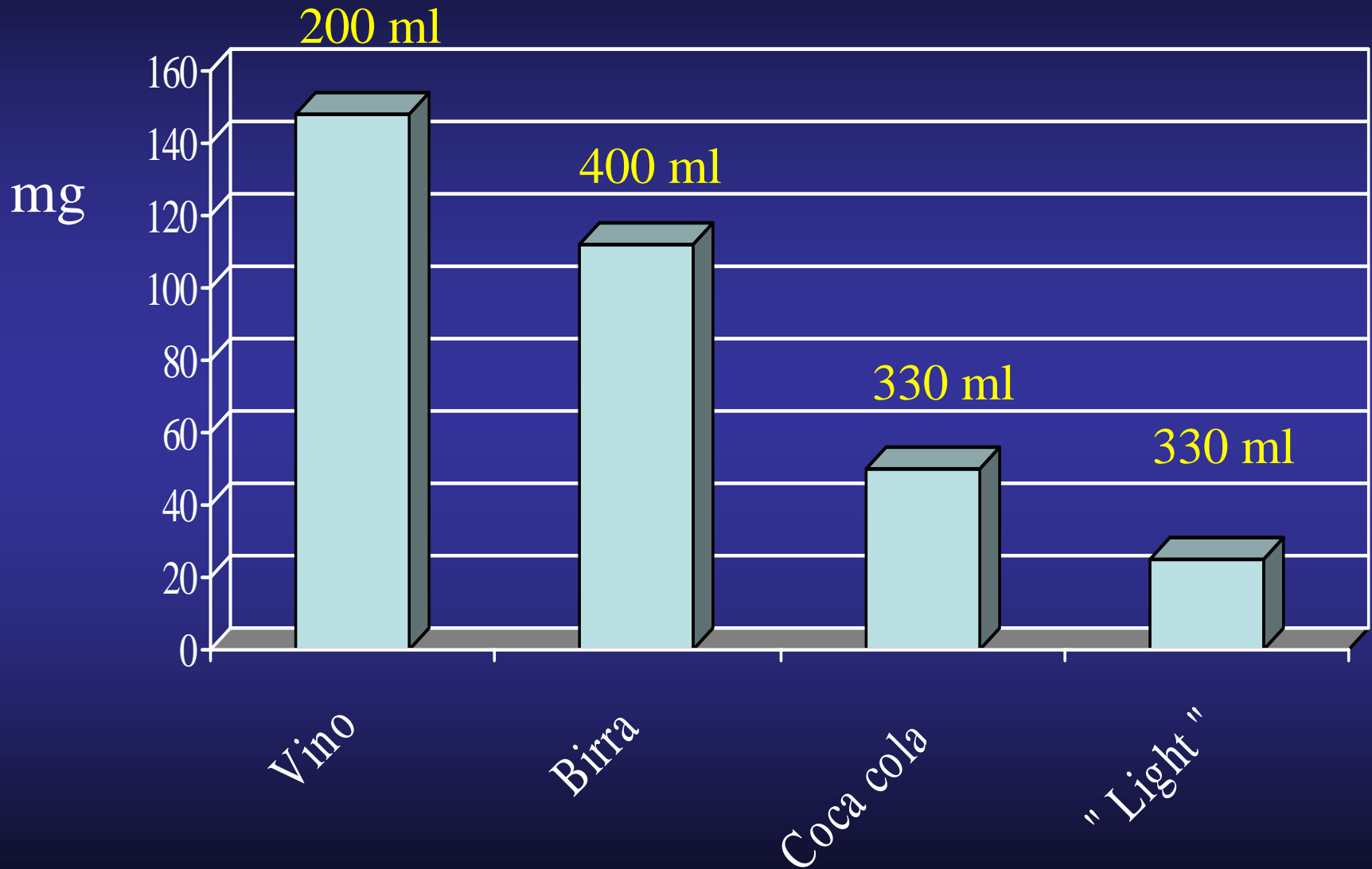




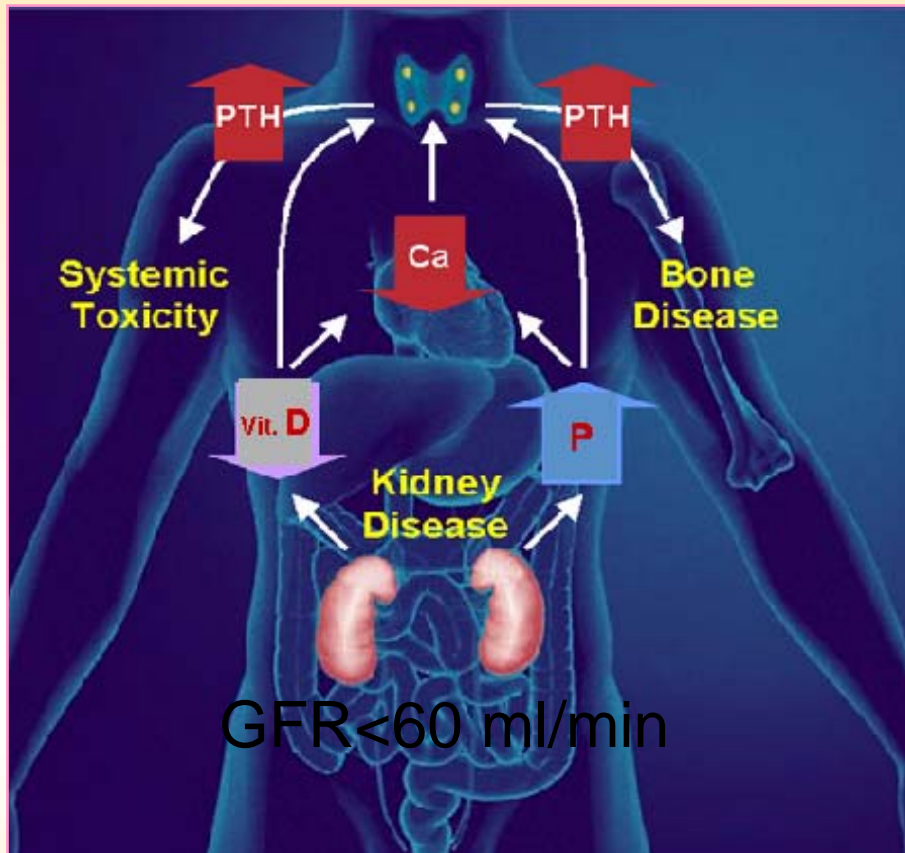




Fosforo nelle bevande



Fisiopatologia delle alterazioni del metabolismo minerale in corso di IRC

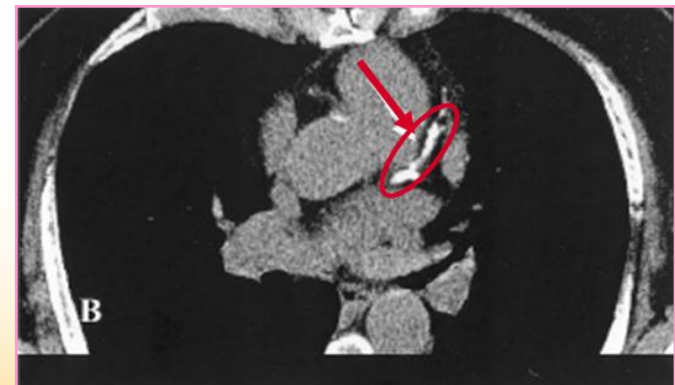
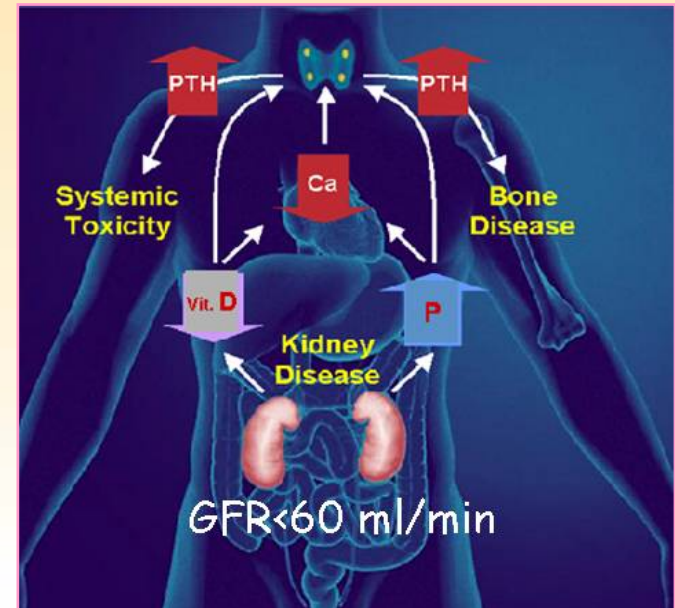


Le prime alterazioni si hanno quando il GFR è <50-60 ml/min. Infatti, gli incrementi del fosforo si osservano già in tale fasi dell'IRC.

CONCLUSIONI

Una precoce restrizione del fosforo risulta pertanto necessaria:

- Per la **prevenzione e la correzione** dell'iperplasia paratiroidea e del conseguente **iperparatiroidismo secondario**.
- Per la **prevenzione delle malattie cardiovascolari**.



Conclusioni

- Una corretta dieta ipoproteica-ipofosforica è efficace nel controllo della fosforemia e nella prevenzione dell'iperparatiroidismo secondario nei pazienti in terapia conservativa
- La manipolazione dietetica da sola non è in grado di controllare l'iperfosforemia nel paziente in dialisi convenzionale, se non con il rischio di malnutrizione proteica