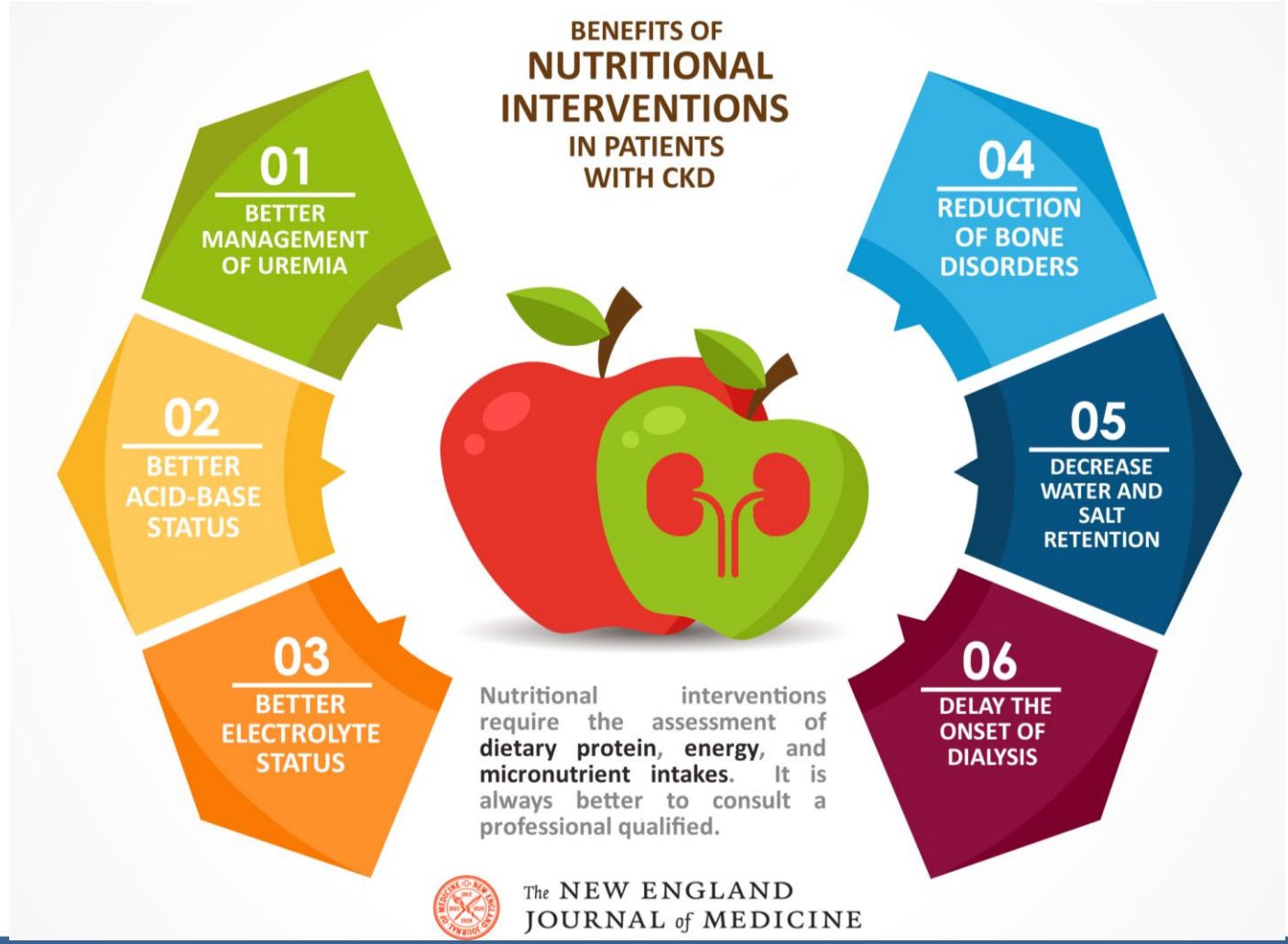
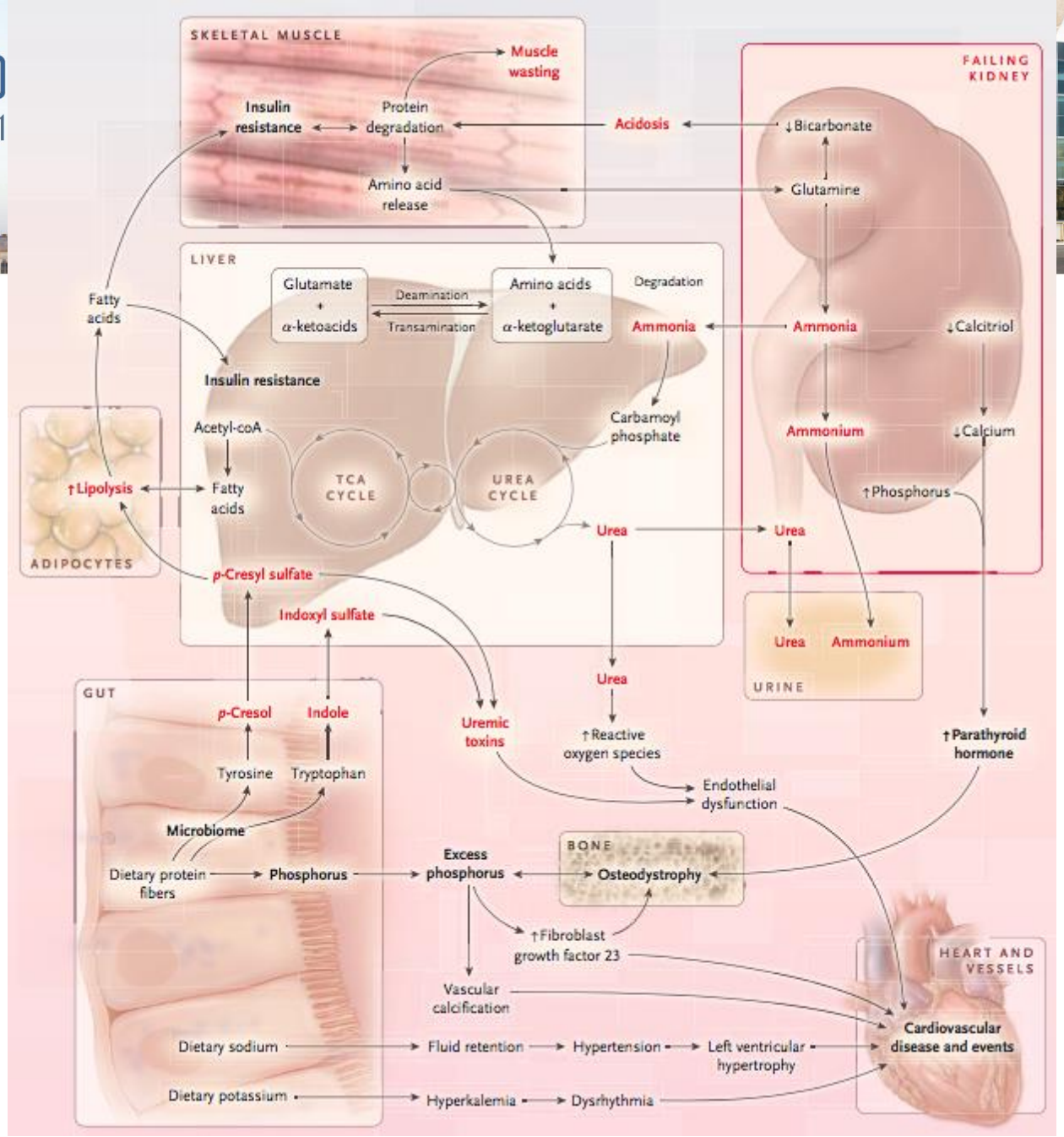

1- 4 OCTOBRE 2019
SESSIONS DPC : 30 SEPTEMBRE - 1 OCTOBRE 2019
4ÈME CONGRÈS DE LA SOCIÉTÉ FRANCOPHONE DE NÉPHROLOGIE, DIALYSE ET TRANSPLANTATION
CENTRE DE CONGRÈS PROUVÉ
NANCY
SFNDT


BENEFITS OF
NUTRITIONAL INTERVENTIONS
IN PATIENTS WITH CKD
01 BETTER MANAGEMENT OF UREMIA
02 BETTER ACID-BASE STATUS
03 BETTER ELECTROLYTE STATUS
04 REDUCTION OF BONE DISORDERS
05 DECREASE WATER AND SALT RETENTION
06 DELAY THE ONSET OF DIALYSIS
Nutritional interventions require the assessment of dietary protein, energy, and micronutrient intakes. It is always better to consult a professional qualified.
The NEW ENGLAND JOURNAL of MEDICINE



Kalantar et al, N Engl J Med 2017;377: 1765-76

Production mondiale de viande et croissance de la population

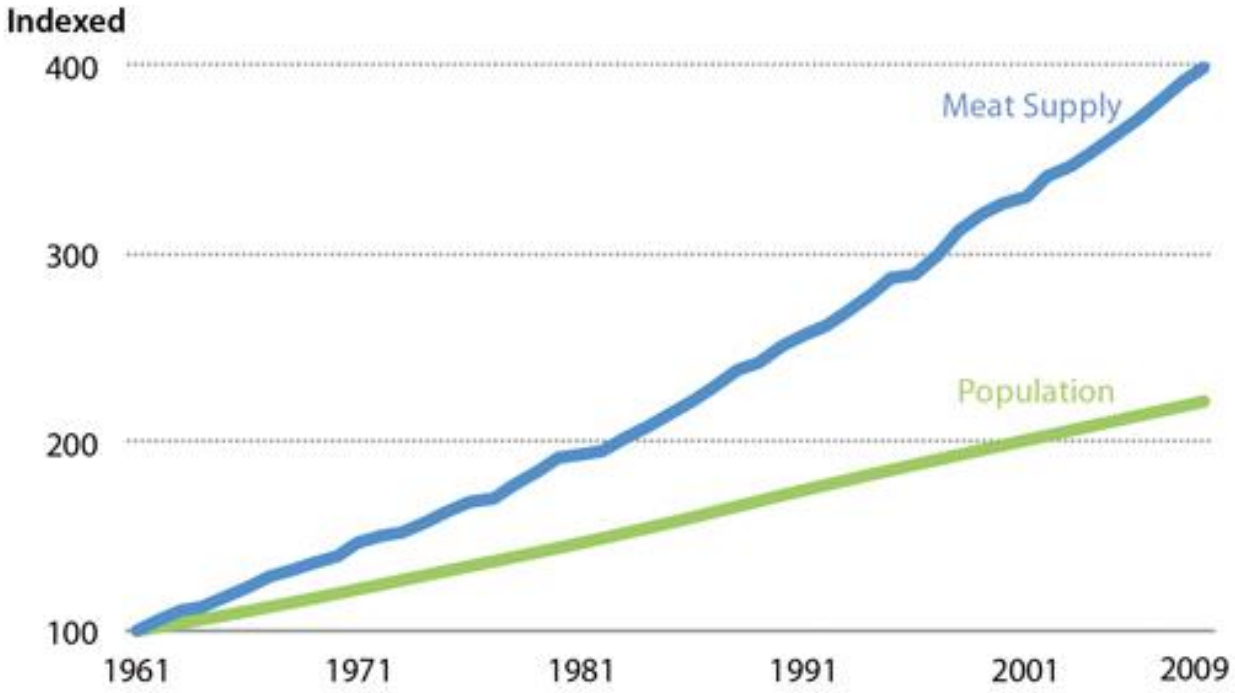


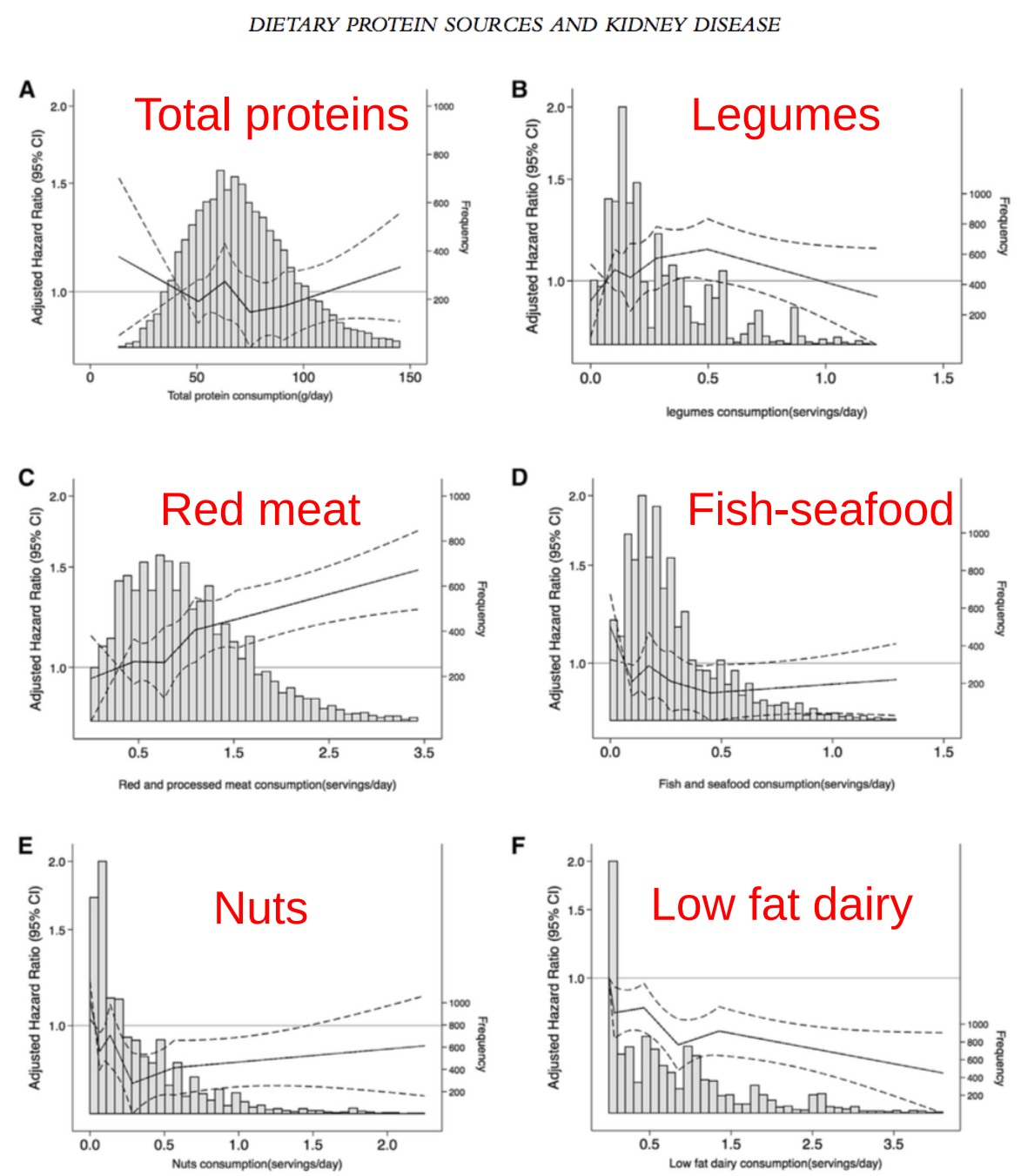
Figure 1: Growth of population and meat supply, indexed 1961=100 (FAO 2012a, UN 2012)

ORIGINAL RESEARCH

Dietary Protein Sources and Risk for Incident Chronic Kidney Disease: Results From the Atherosclerosis Risk in Communities (ARIC) Study

Bernhard Haring, MD, MPH, Elizabeth Selvin, PhD, MPH,†'‡ Menglu Liang, ScM, MPH,†'‡ Josef Coresh, MD, PhD, MHS,†'‡ Morgan E. Grams, MD, PhD, MHS,†'§ Natalia Petruski-Ivleva, MS,¶ Lyn M. Steffen, PhD, MPH, RD,** and Casey M. Rebholz, PhD, MS, MPH†'‡*

Journal of Renal Nutrition 27; 2017:233-242



Incident chronic kidney disease in more than 15,000 adults of the ARIC study

Harring et al; J Renal Nutr 27, 2017:233-242

Apports nutritionnels en population générale

Adultes en bonne santé, pays occidentaux

- 1.3 – 1.4 g prot/kg/j
- 35 - 40 kcal/kg/j
- 9 -12 g NaCl/j
- 1200 - 1800 mg phosphate
- 1000 mg calcium

Apports protéiques moyens à différents stades de la MRC

Table 2 | Unadjusted dietary protein intake of participants from NHANES 2001–2008, according to the level of kidney function

Parameter	NoCKD	Stage 1	Stage 2	Stage 3	Stage 4+[a]
Dietary protein intake, g/day[b]					
Mean ± s.e. (s.d.$_{CS}$)	86.1 ± 0.8 (43.6)	78.8 ± 2.3 (43.3)	77.8 ± 2.0 (45.3)	69.0 ± 1.4 (34.8)	60.1 ± 2.4 (27.7)
P-value	Ref[c]	0.0025	<0.0001	<0.0001	<0.0001
Dietary protein intake, g/kg IBW/d[e]					
Mean ± s.e. (SD$_{CS}$)	1.34 ± 0.01 (0.62)	1.32 ± 0.04 (0.71)	1.26 ± 0.03 (0.69)	1.14 ± 0.02 (0.52)	1.04 ± 0.05 (0.49)
P-value[b]	Ref[c]	0.2565	0.0002	<0.0001	<0.0001
High biological value, % of total DPI[f,g]					
Mean ± s.e. (s.d.$_{CS}$)	58.2 ± 0.3 (23.2)	60.2 ± 1.2 (22.9)	57.5 ± 1.0 (23.4)	60.0 ± 0.9 (21.9)	62.9 ± 2.1 (19.4)
P-value	(Ref)‡	0.1122	0.6210	0.0341	0.0279

Moore et al. Kidney Int 2013;83:724

CKD progression

Proteinuria

Uremia management and deferral of dialysis

Metabolic acidosis

Mineral and bone disease

PEW

Cardiovascular and metabolic health

Glycemic control and insulin response

Quality of life and adherence to LPD

Mortality

Hypertension management

Microbiome modulation

Patients MRC doivent réduire leurs apports en protéines: 12 points essentiels

Kalantar et al, N Engl J Med 2017;377: 1765-76

Apports protéiques aggravent la pathologie rénale

casein	45%	30%	20%
Proteinuria (mg/day)	186 ±23	248 ±32	141 ±42 *
S insulin	14.6 ±1.9	12.0 ±1.4	11.7 ±1.9 *

Renal expression

casein	45%	30%	20%
SREBP1	2.2 ±0.2	2.2 ±0.2	1.0 ±0.2 *
TNF-alpha	3.5 ±0.6	2.7 ±0.4	1.1 ±0.3 *
IL-6	2.1 ±0.3	2.0 ±0.2	1.0 ±0.1 *
IV collagen	1.65 ±0.2	2.0 ±0.3	1.0 ±0.2 *
TGF-beta	1.9 ±0.2	1.4 ±0.2	1.0 ±0.1 *

Lipides

inflammation

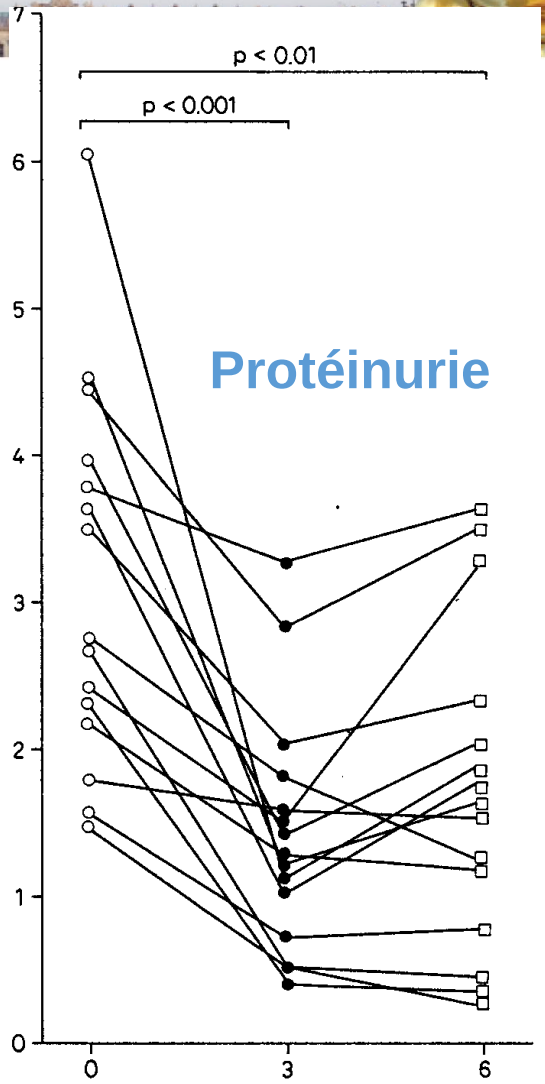
Expansion matricielle

fibrose

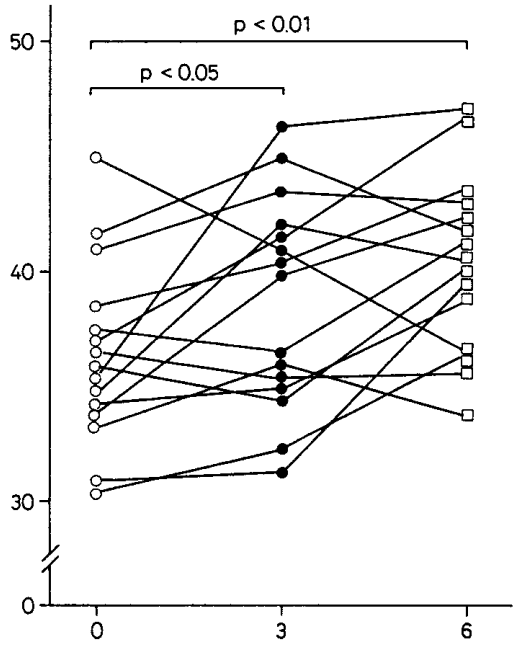
Tovar-Palacio et al, Am J Physiol 2011 300:F263

0.3 g prot/kg + ketoacides

Protéinurie

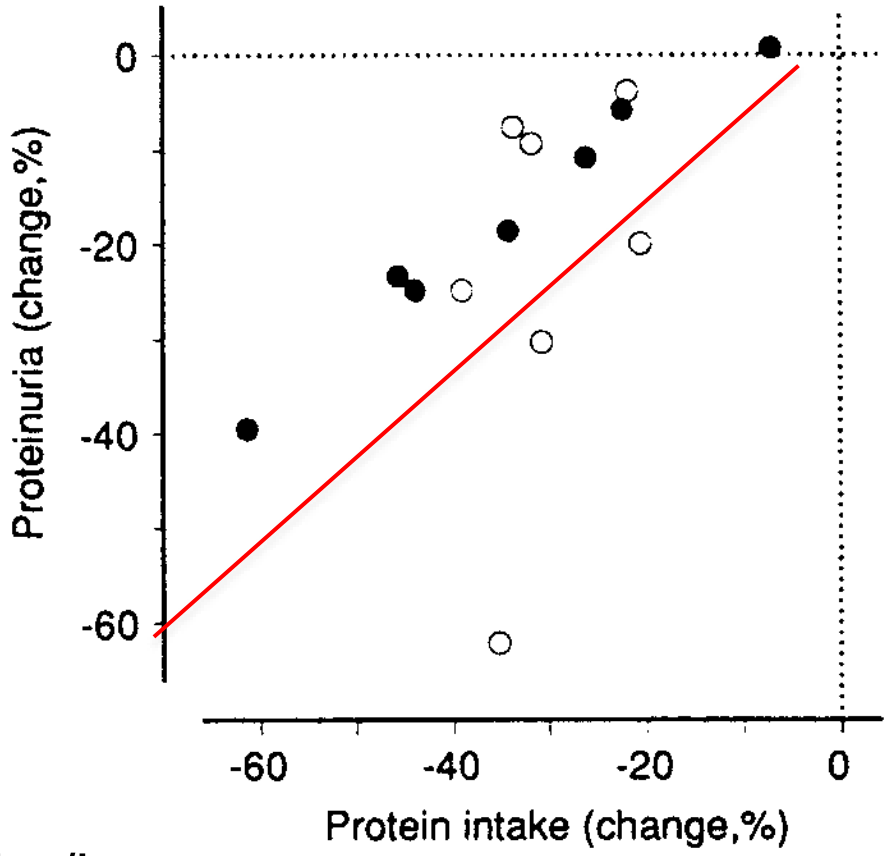


Albuminémie



Réduire les apports protéiques réduit la protéinurie

Aparicio et al, Nephron 1988



Réduction proportionnelle des apports protéiques et de la protéinurie

Apport protéique basal ≥ 1 g/kg/j

Gansevoort et al, NDT 1992

Réduction de l'urée plasmatique

(l'urée est-elle toxique?)

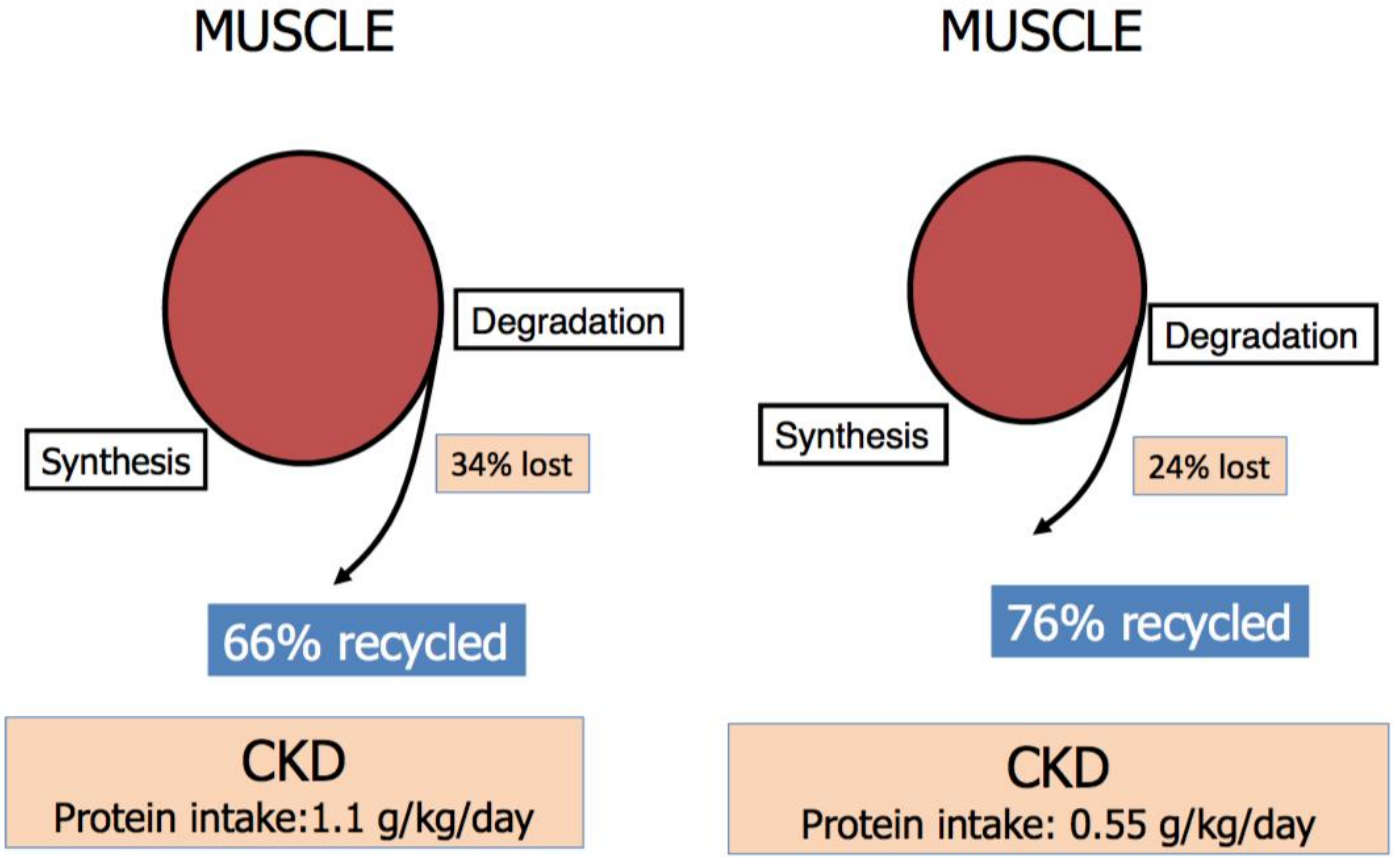
Koppe et al, J Clin Invest 2016, 126:3598 *Urea impairs β cell glycolysis and insulin secretion in chronic kidney disease.*

Après 3 mois à 0.3 g/kg/j + ketoanalogues

	Before	After
Serum creatinine (μmol/L)	463 ± 37	438 ± 62
GFR (mL/min)	13.2 ± 2.8	10.8 ± 2.0
Plasma urea (mmol/L)	24.3 ± 1.8	10.6 ± 1.7[2]
Urinary urea (mmol/d)	171 ± 10	68 ± 5[2]
Uric acid (μmol/L)	556 ± 31	405 ± 30[3]
Total calcium (mmol/L)	2.29 ± 0.07	2.38 ± 0.06
Phosphorus (mmol/L)	1.45 ± 0.22	1.34 ± 0.10
PTH (ng/L)	273 ± 139	172 ± 86
Arterial pH	7.39 ± 0.01	7.40 ± 0.01
Arterial bicarbonate (mmol/L)	24.2 ± 1.2	24.5 ± 1.3
Triacylglycerol (mmol/L)	2.7 ± 0.6	2.1 ± 0.4
Cholesterol (mmol/L)	6.3 ± 0.7	5.1 ± 0.4

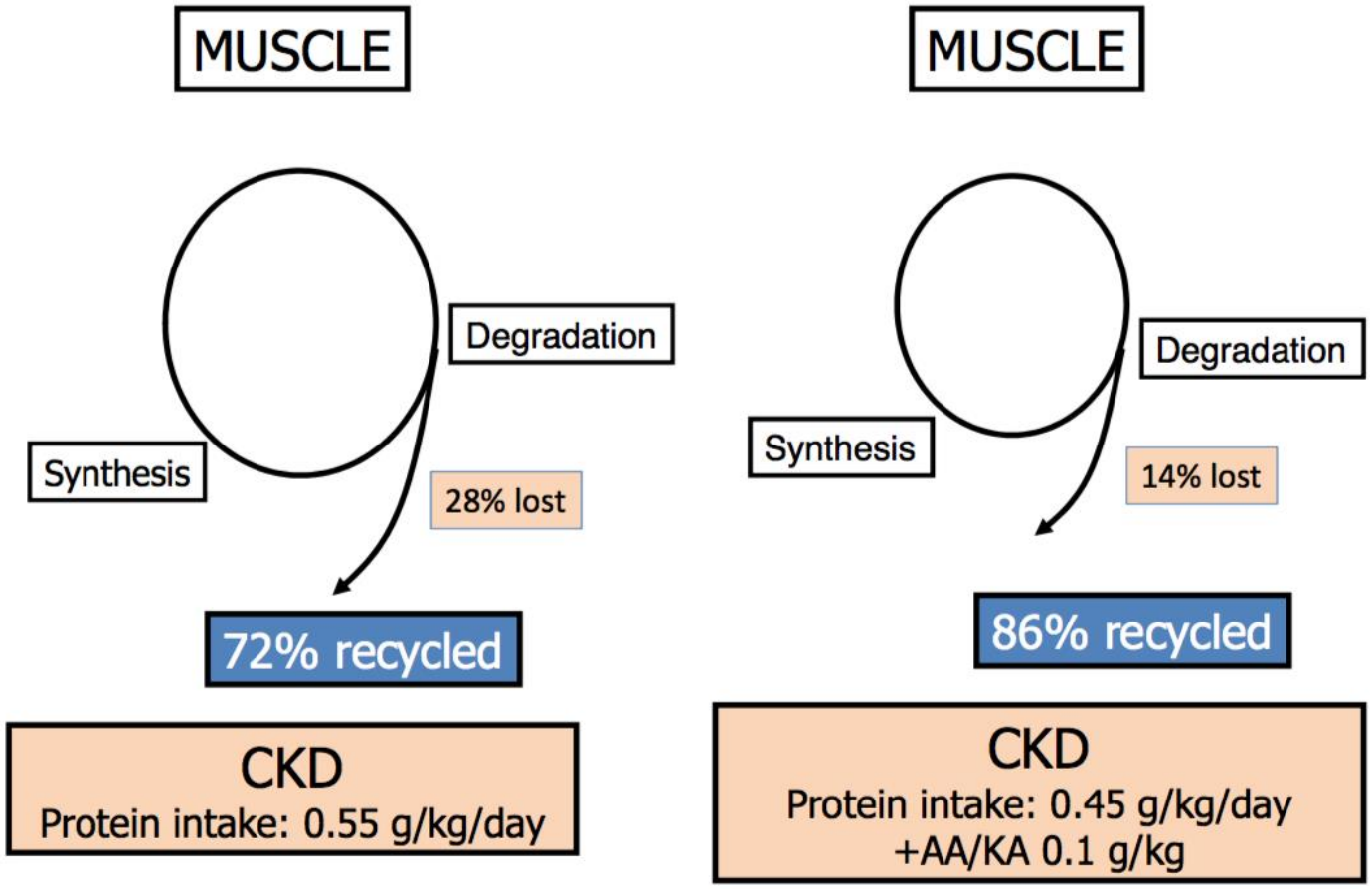
Rigalleau et al. Am J Clin Nutr 1997

Cinétique musculaire de la phénylalanine, patients MRC



Garibotto et al, KI reports 2018;3:701-710

Cinétique musculaire de la phénylalanine, patients MRC



Garibotto et al, KI reports 2018;3:701-710

Insulinoresistance

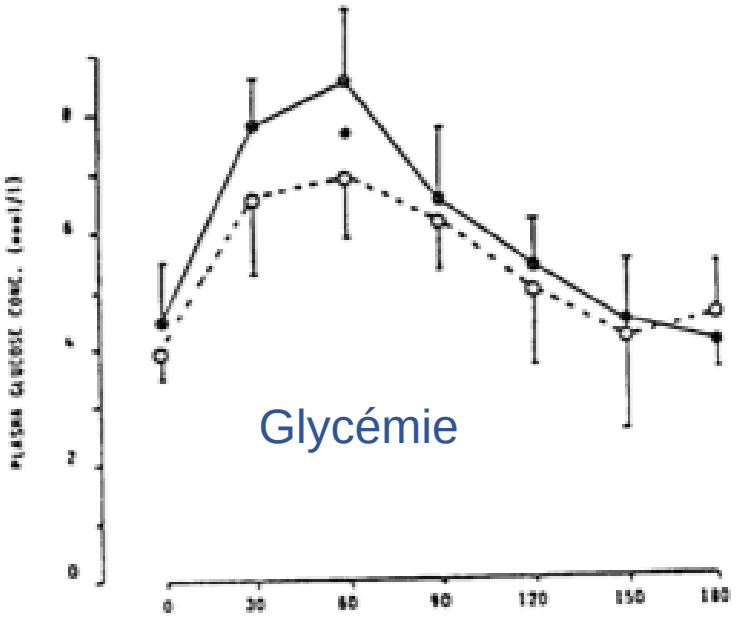
Apports protéiques réduits de 1 g/kg/j à 0.3g + cétoanalogues pdt 4 mois

↓

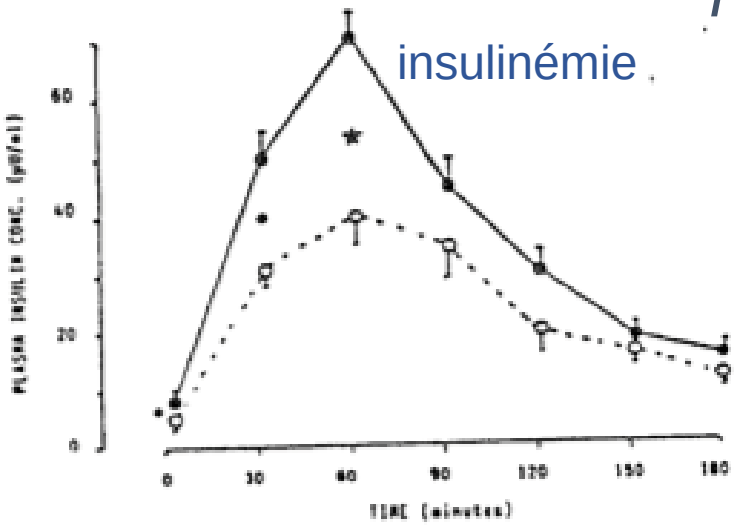
Amélioration de la glycémie et de l'insulinorésistance

↑

Adipocyte



HGP



Gin et al. Metabolism 1987

Carnitine et TMAO

JCI The Journal of Clinical Investigation

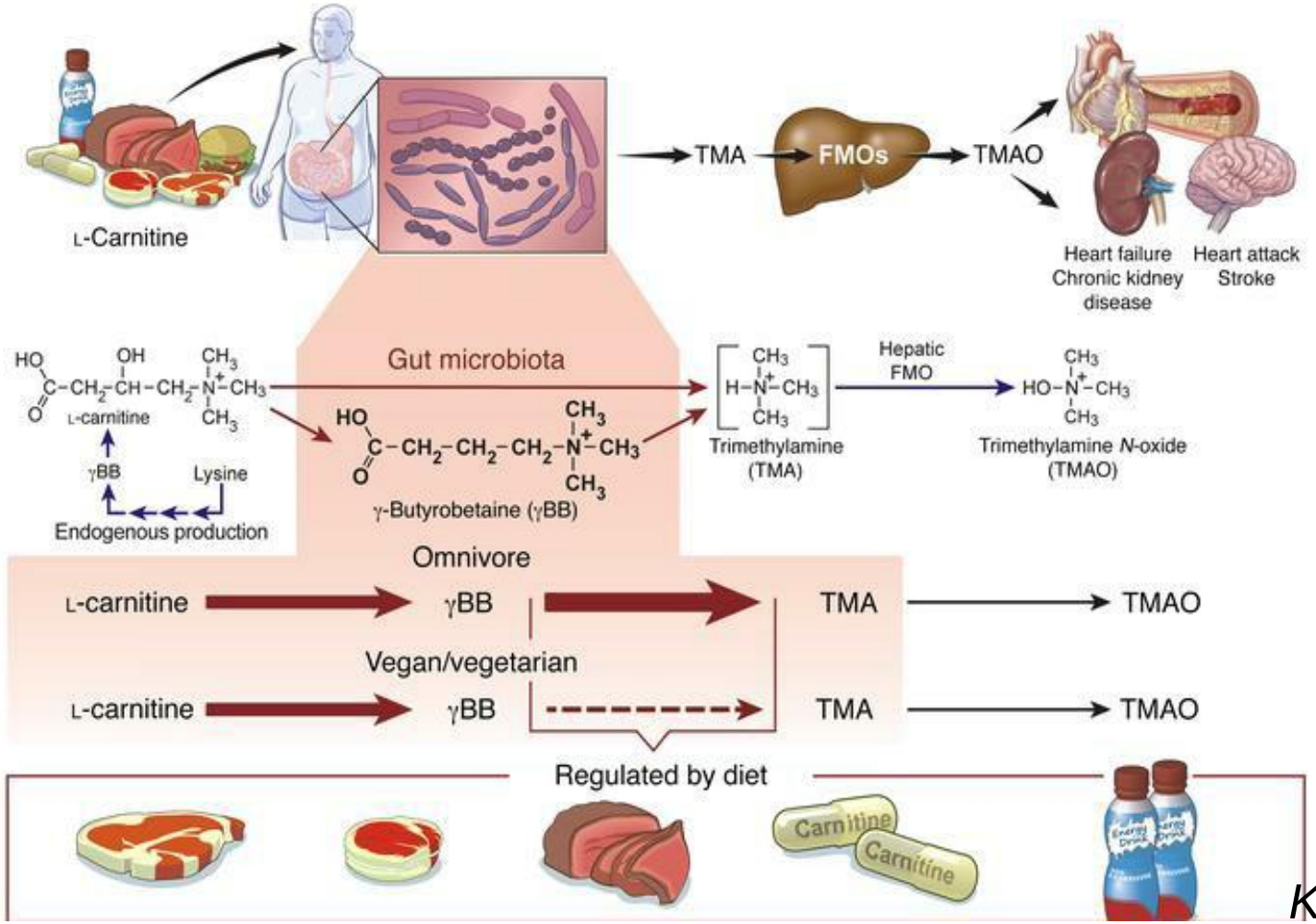
l-Carnitine in omnivorous diets induces an atherogenic gut microbial pathway in humans

Robert A. Koeth, … , Jose Carlos Garcia-Garcia, Stanley L. Hazen

La carnitine alimentaire est associée à un microbiote athérogène

Koeth et al, JCI 2018

- Tous transforment la carnitine en BB
- Omnivores transforment BB en TMA
- Végétariens: pas de TMA
- Un régime riche en viande rouge induit un microbiote athérogène



Koeth et al, JCI 2018

Réduction des apports de phosphate

De 15 à 8 mg/kg/j (apport régulier de1500 mg/j)

TABLE 1
Biochemical and physiologic indexes before and after 3 mo of a low-protein diet[1]

	Before	After
Serum creatinine (μmol/L)	463 ± 37	438 ± 62
GFR (mL/min)	13.2 ± 2.8	10.8 ± 2.0
Plasma urea (mmol/L)	24.3 ± 1.8	10.6 ± 1.7[2]
Urinary urea (mmol/d)	171 ± 10	68 ± 5[2]
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Cholesterol (mmol/L)	6.3 ± 0.7	5.1 ± 0.4

Rigalleau et al. Am J Clin Nutr 1997

Nature des protéines et effets métaboliques

- 2938 adultes de l'étude CRIC
- Consommation habituelle par enquêtes (FFQ)
- Distinction entre protéines animales et végétales
- Apport protéique moyen de 63.7 g/j
  - Animales: 41.8 g/j
  - Plantes 20.7 g/j
  - Pourcentage de protéines végétales: 33% (IQR 26-41%)

Scialla et al. J Renal Nutr, 2012; 22: 379-388.

Nature des protéines et effets métaboliques

Unadjusted mean values (± standard deviation) of metabolic parameters by quintiles of percent plant protein

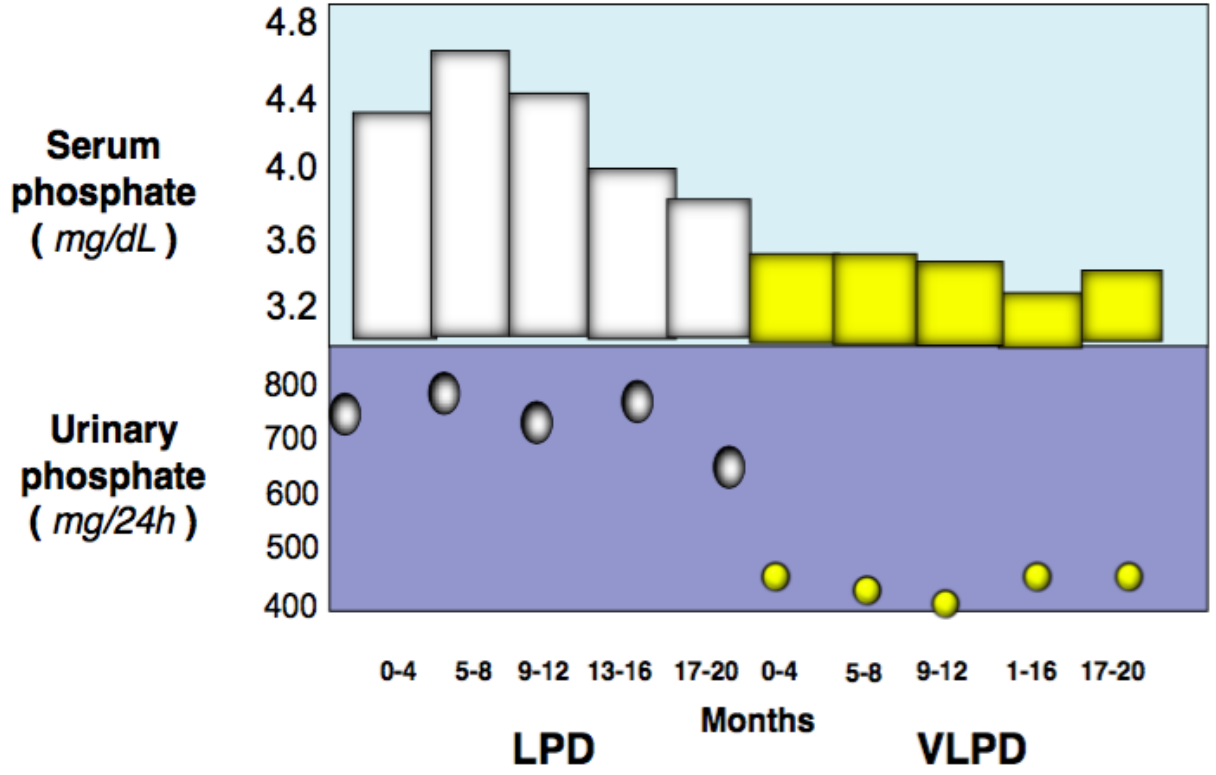
	1 <24% (n=587)	2 24–29% (n=588)	3 30–35% (n=588)	4 36–44% (n=587)	5 >44% (n=588)	p-trend
Serum phosphate (mg/dL)	3.67 ± 0.66	3.73 ± 0.64	3.69 ± 0.65	3.69 ± 0.61	3.69 ± 0.66	0.69
FGF23 (RU/mL) †	138 (92, 239)	144 (95, 247)	143 (94, 224)	139 (95, 232)	134 (88, 215)	0.60
24 urinary phosphate (mg)	849 ± 369.96	812 ± 363.71	768 ± 347.17	752 ± 318.22	697 ± 331.06	<0.001
iPTH (pg/mL) †	53 (34, 87)	54 (33, 90)	51 (33, 83)	53 (34, 84)	52 (35, 84)	0.83
Serum bicarbonate (mEq/L)	24.47 ± 3.17	24.50 ± 3.05	24.50 ± 3.07	24.85 ± 3.22	24.82 ± 3.19	0.07

† Median (interquartile range)

FGF23 = fibroblast growth factor 23; iPTH = intact parathyroid hormone

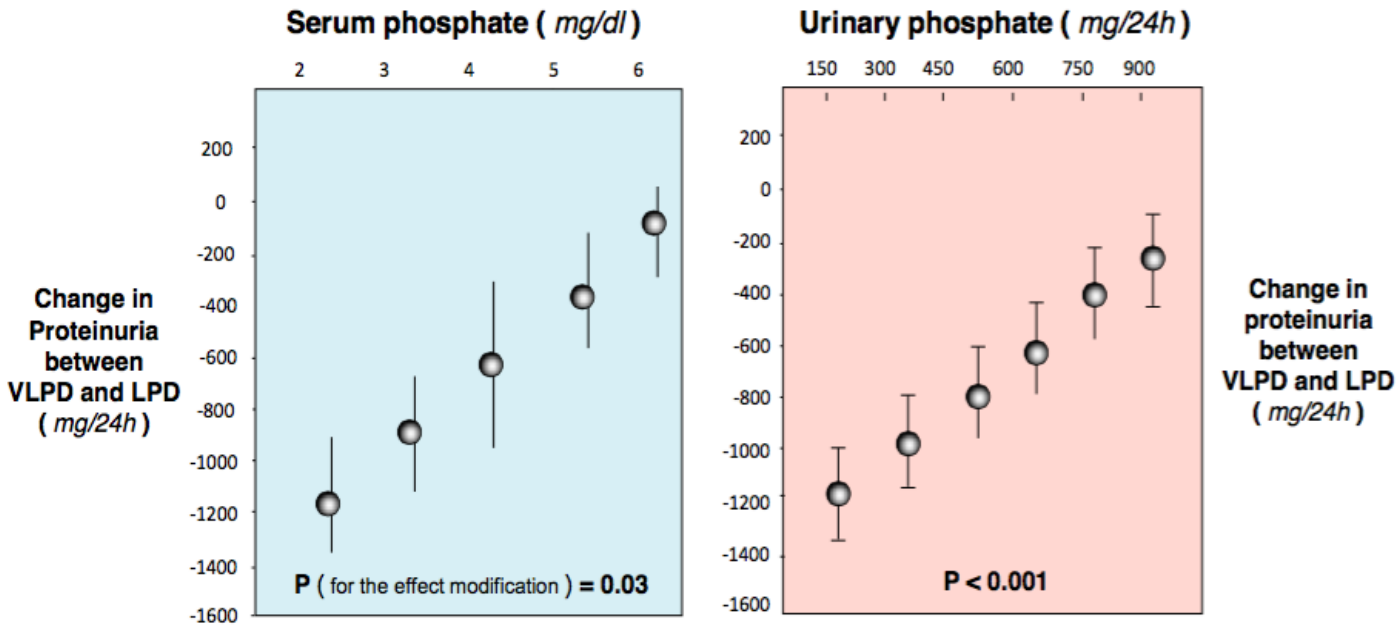
Scialla et al. J Renal Nutr, 2012; 22: 379-388.

Phosphatémie et phosphaturie



Di Iorio, Bellizzi, *Nephrol Dial Transplant* 2013

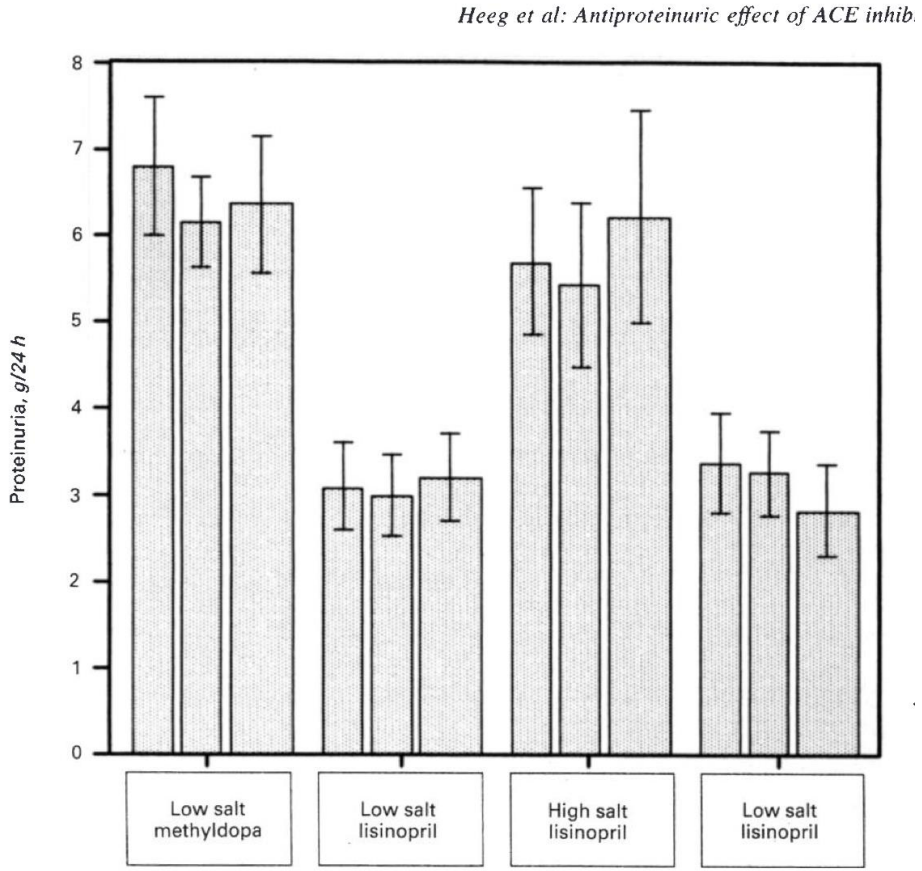
Phosphatémie, phosphaturia et réponse antiprotéinurique aux IEC



Phosphate burden is an effect modifier for the anti-proteinuric response to very low protein diet

Di Iorio, Bellizzi, *Nephrol Dial Transplant* 2013

Sel, IEC et protéinurie



Heeg Kidney Int 1987

Apports en potassium et kaliémie

- Pas d'augmentation de la kaliémie au cours d'un régime riche en fruits et légumes
- C'est la constipation qui est facteur de risque d'hyperkaliémie et non les apports en potassium

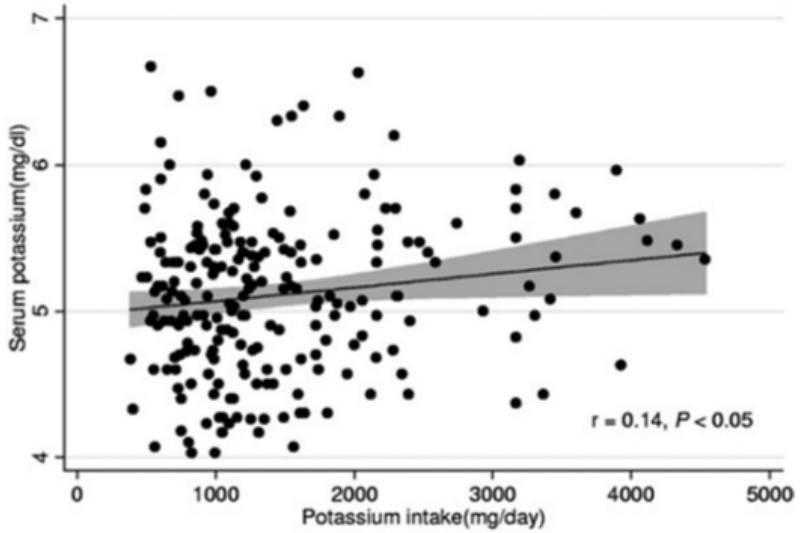


Figure 1. Associations of reported dietary potassium intake with serum potassium concentration in hemodialysis patients from the Nutritional and Inflammatory Evaluation in Dialysis study (n = 224). Regression line (solid line) and 95% confidence interval (shadedarea) are shown for the linear regression analysis. Reproduced with permission from Noori et al., Am J Kidney Dis 2010;56(2):338-347.

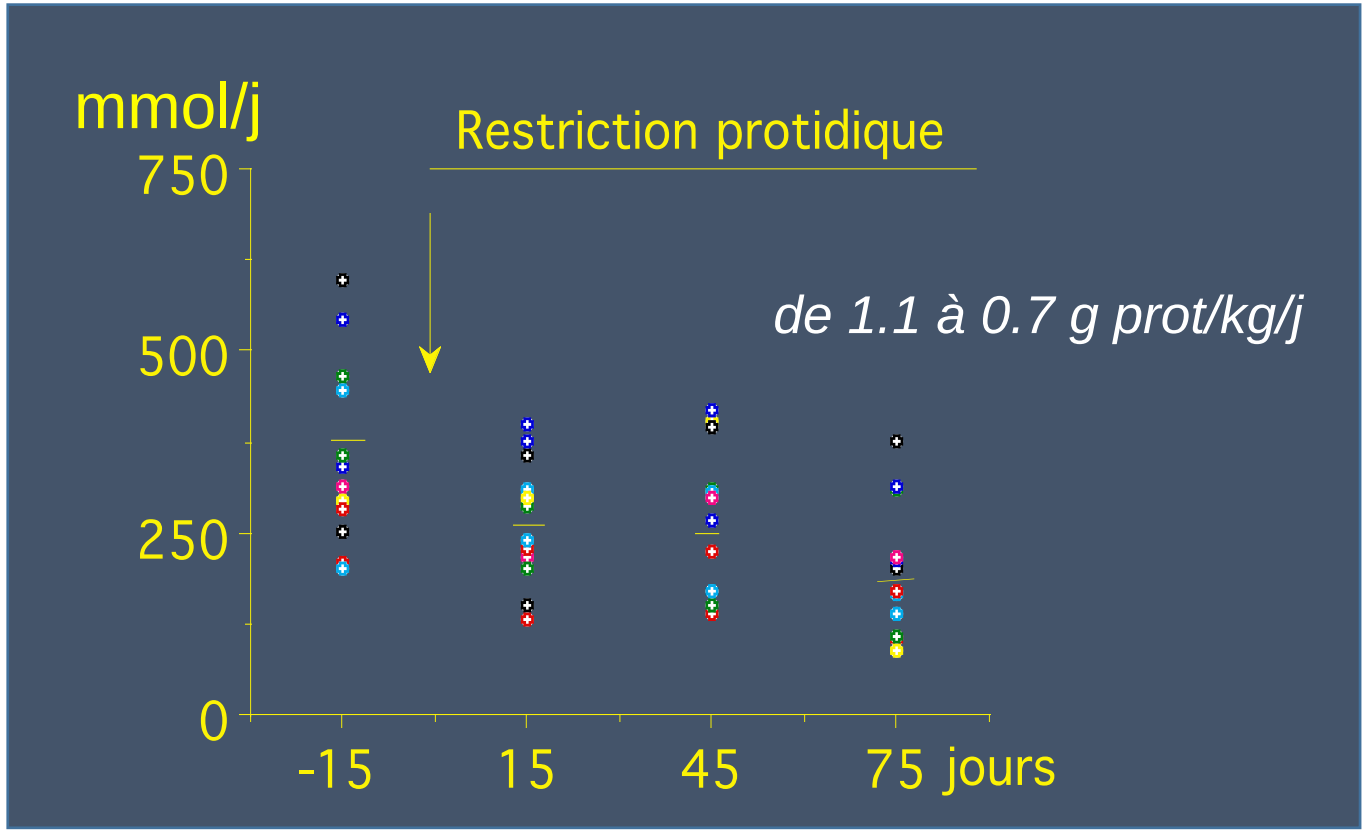
NIED study, 224 MHD pts

St-Jules et al, J Renal Nutr 2016; 26:282

Suivi de l'observance: Urée urinaire de 24h

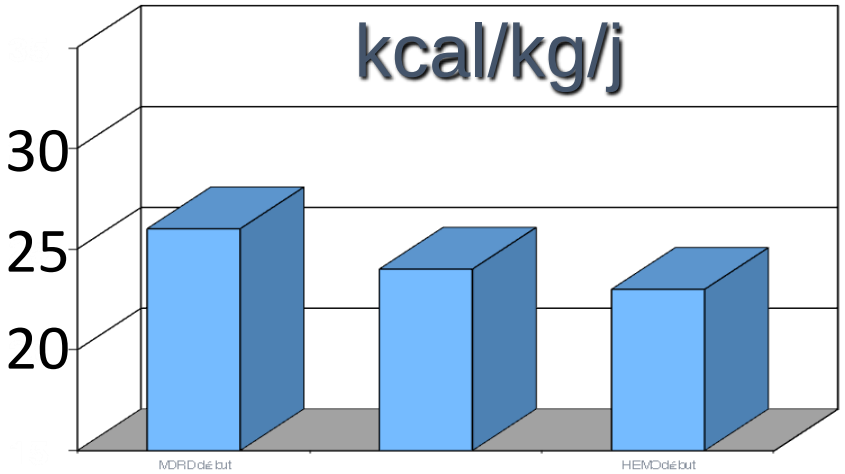
Observance:

- entre 30 et 66% des patients
- Garneata (JASN 2016): 15%



Fouque et al. J Am Soc Nephrol 1995

Attention: risque de carence énergétique

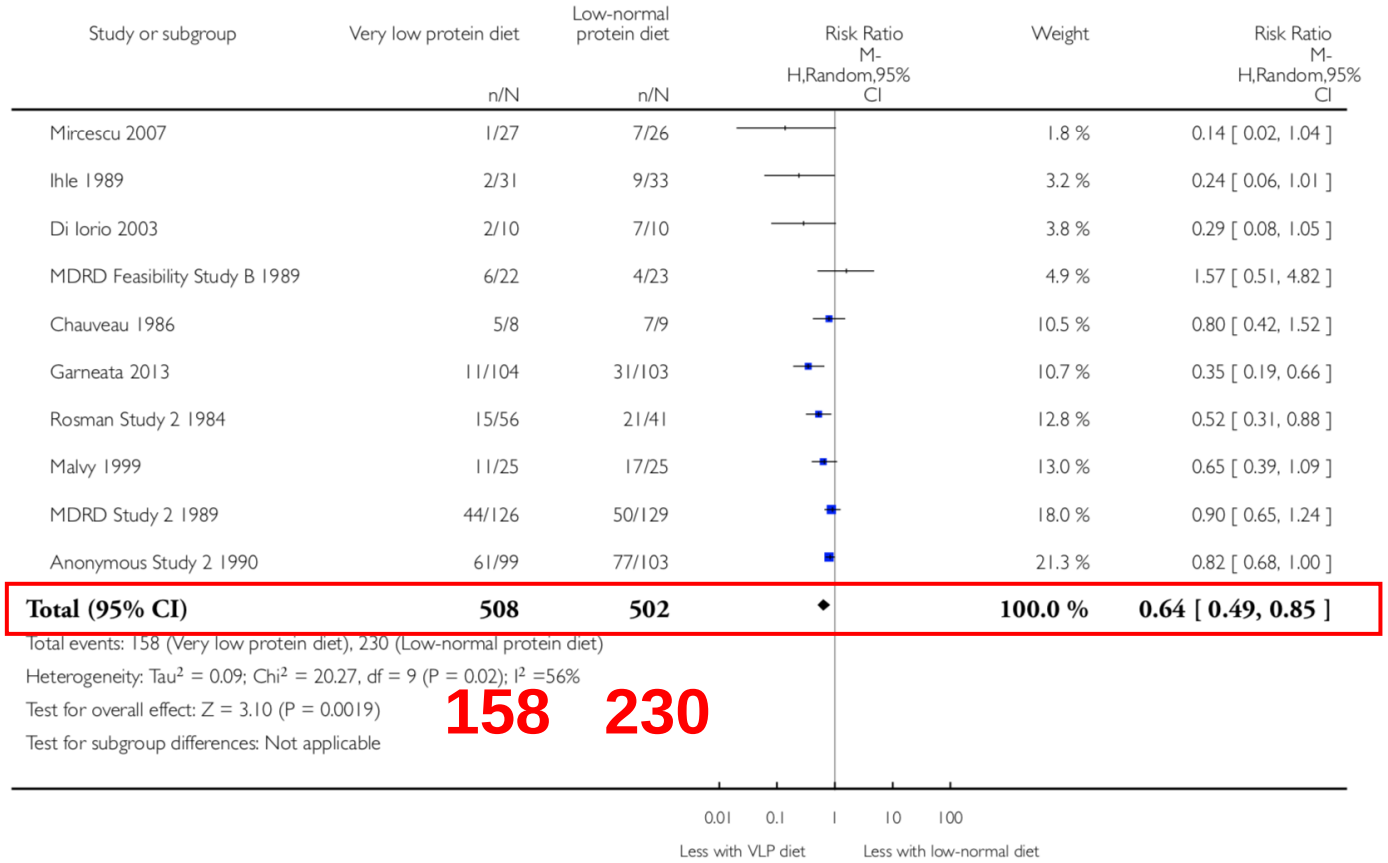


1988 **1993** **1996**

MDRD start MDRD end HEMO start

Cochrane systematic review and meta-analysis

Very low protein diet - end stage kidney disease

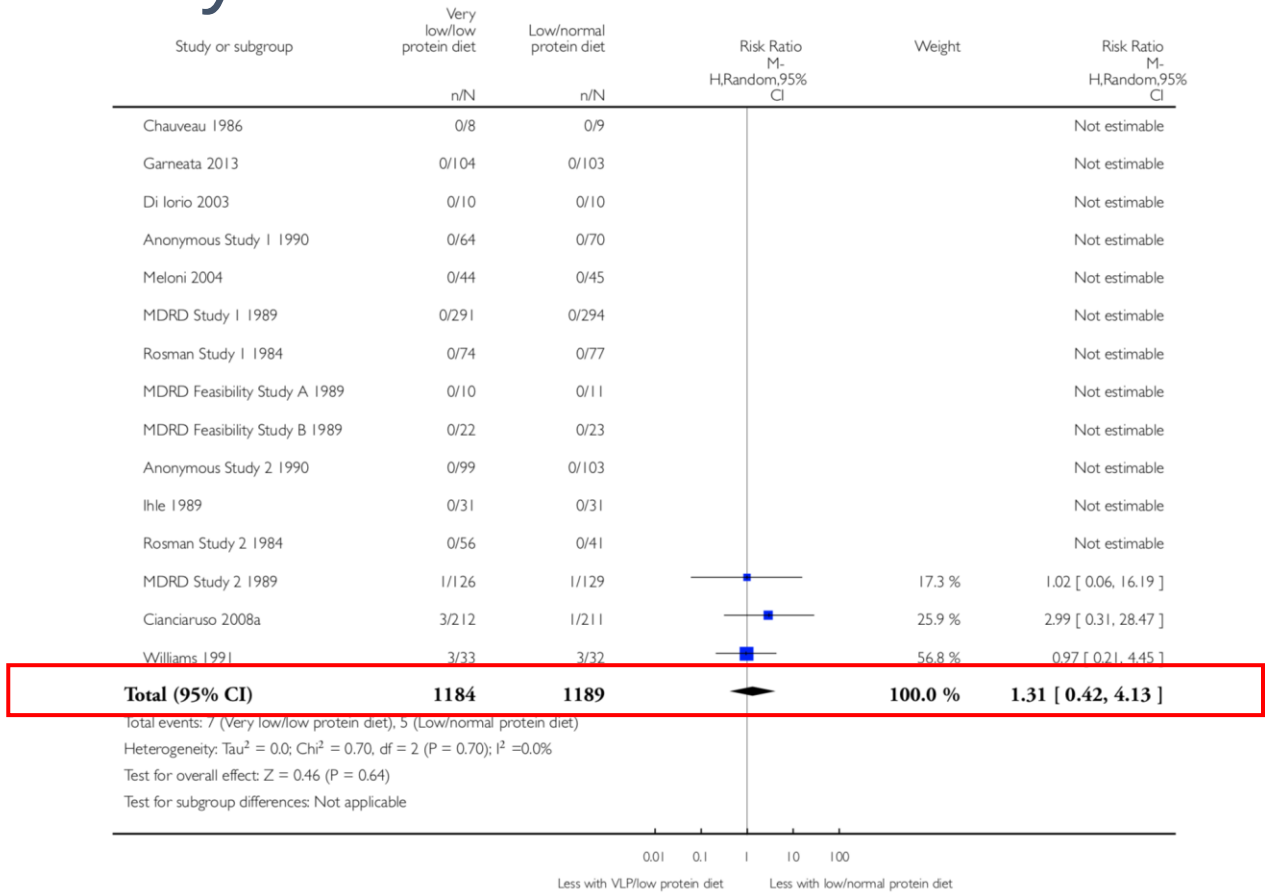


Fouque et al, Cochrane Database Syst Rev Oct 2018

Cochrane systematic review and meta-analysis

Dénutrition ?

Non !



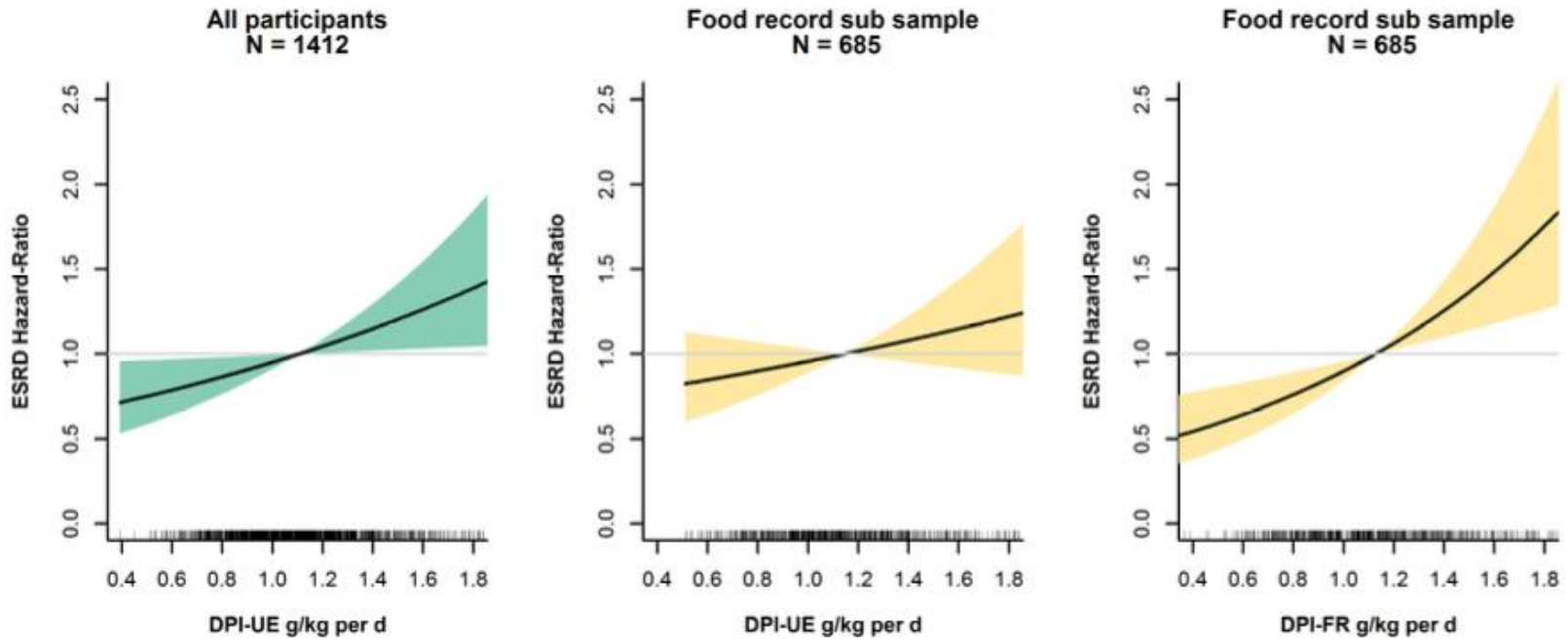
Study or subgroup	Very low/low protein diet n/N	Low/normal protein diet n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Chauveau 1986	0/8	0/9			Not estimable
Garneata 2013	0/104	0/103			Not estimable
Di Iorio 2003	0/10	0/10			Not estimable
Anonymous Study 1 1990	0/64	0/70			Not estimable
Meloni 2004	0/44	0/45			Not estimable
MDRD Study 1 1989	0/291	0/294			Not estimable
Rosman Study 1 1984	0/74	0/77			Not estimable
MDRD Feasibility Study A 1989	0/10	0/11			Not estimable
MDRD Feasibility Study B 1989	0/22	0/23			Not estimable
Anonymous Study 2 1990	0/99	0/103			Not estimable
Ihle 1989	0/31	0/31			Not estimable
Rosman Study 2 1984	0/56	0/41			Not estimable
MDRD Study 2 1989	1/126	1/129		17.3 %	1.02 [0.06, 16.19]
Cianciaruso 2008a	3/212	1/211		25.9 %	2.99 [0.31, 28.47]
Williams 1991	3/33	3/32		56.8 %	0.97 [0.21, 4.45]
Total (95% CI)	**1184**	**1189**		**100.0 %**	**1.31 [0.42, 4.13]**

Total events: 7 (Very low/low protein diet), 5 (Low/normal protein diet)
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.70$, $df = 2$ ($P = 0.70$); $I^2 = 0.0\%$
Test for overall effect: $Z = 0.46$ ($P = 0.64$)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Less with VLP/low protein diet
Less with low/normal protein diet

Fouque et al, Cochrane Database Syst Rev Oct 2018

Nephrotest Paris



1412 patients MRC st 3, suivi 3.5 ans

Metzger et al, Kidney Int reports 2018

Aspects économiques des apports très réduits en protéines

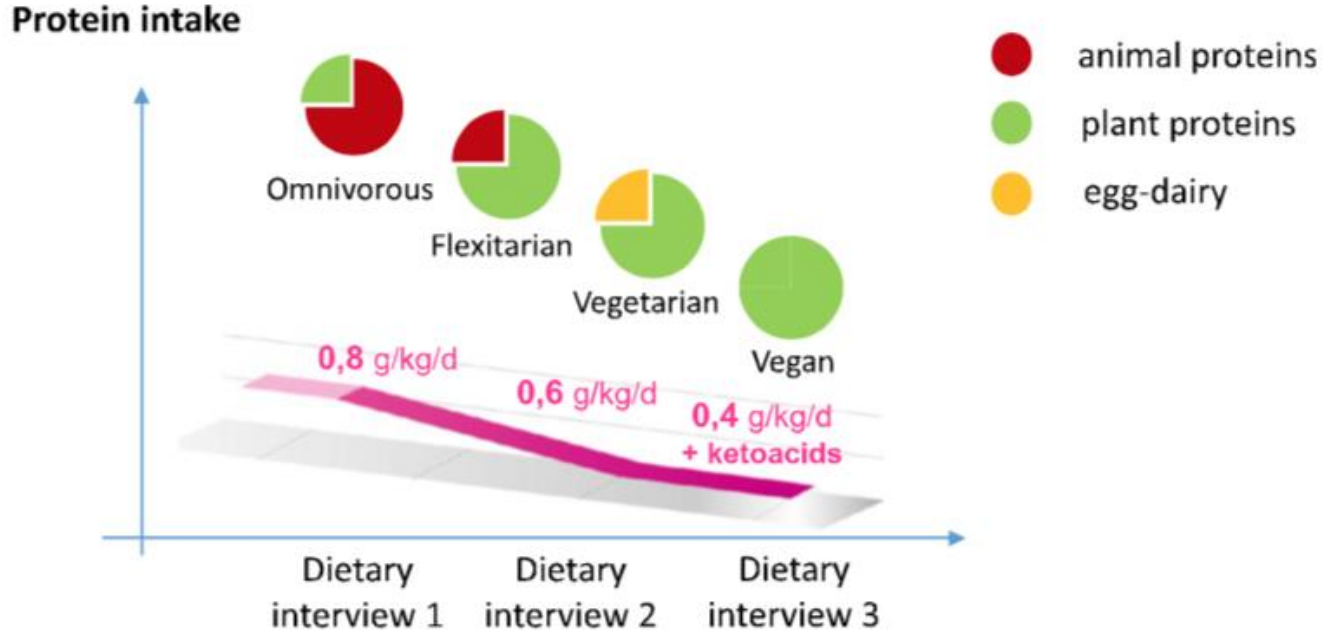
- Italie: MRC st IV et > 40 ans= 100 000 pts
- Modèle de Markov
- Basé sur la revue Cochrane (Fouque et al, 2009)
- 702 patients: 351 LPD vs 351 SVLPD
- Décès et dialyse

34 000 € vs 1440 € (coût annuel)

A l'heure de la mise en place de la forfaitisation des st IV et V en France

Mennini et al., J Renal Nutr 2014;24:313-321

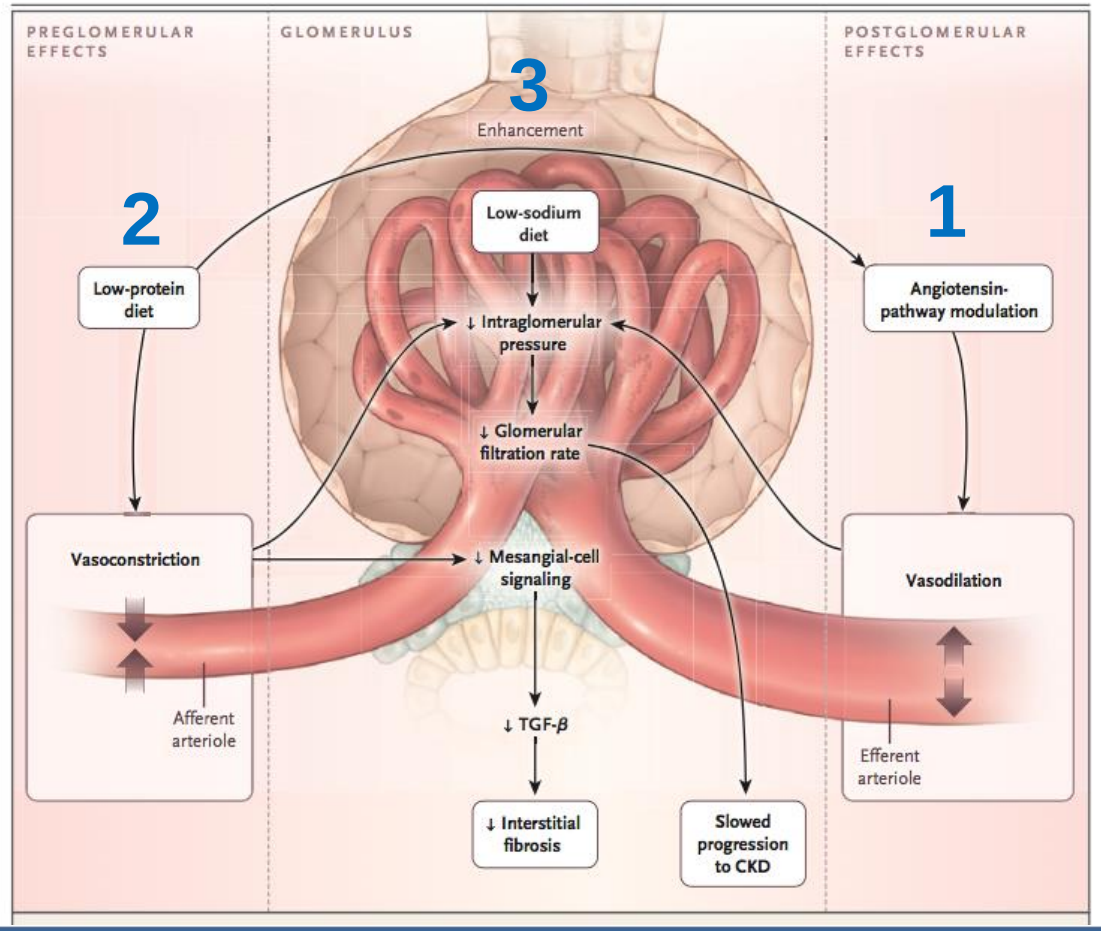
Comment proposer un régime réduit en protéines?



- Progressively decrease by 0.2 g/kg/d with the help of 3 dietary encounters
- Coach and measure compliance to reach the prescribed target

Wang et al, Semin Nephrol 2018;4:383

Impacts de l'intervention nutritionnelle en MRC



Kalantar et al, N Engl J Med 2017;377: 1765-76

Journal of Renal Nutrition
National Kidney Foundation
INTERNATIONAL SOCIETY OF RENAL NUTRITION AND METABOLISM

CONSENSUS STATEMENT

Keto Acid Therapy in Predialysis Chronic Kidney Disease Patients: Final Consensus

Stage	eGFR (mL/minute/1.73 m^2)	Considered Daily Protein Supply
1	≥90	Normal protein intake (RDA: 0.8 g protein/kg body weight/day)
2	60-89	Normal protein intake (RDA: 0.8 g protein/kg body weight/day)
3	30-59	
	a. 45-59 (with increasing serum creatinine)	Normal protein intake (RDA: 0.8 g protein/kg body weight/day)
	b. 30-44 (with increasing serum creatinine)	Protein restriction 0.6/0.7 g protein/kg body weight/day
4	15-29 (with increasing serum creatinine)	Protein restriction 1. 0.6 g protein/kg body weight/day 2. 0.3-0.4 g protein/kg body weight/day
5	<10-15 (not on dialysis)	Protein restriction 1. 0.6 g protein/kg body weight/day 2. 0.3-0.4 g protein/kg body weight/day

low-normal protein low sodium
low phosphate, normal energy

Improve CKD-MBD, BP, proteinuria

Slow renal progression

low protein low sodium low phosphate
low acids increase energy

reduce uremic toxicity
improve uremic symptoms
reduce protein-energy wasting

delay ESRD

J Renal Nutr, Vol 22, 2012: pp S22-S24