Utilità per il controllo dell'uremia in fase conservativa: le nuove KDOQI Nutrition Guidelines

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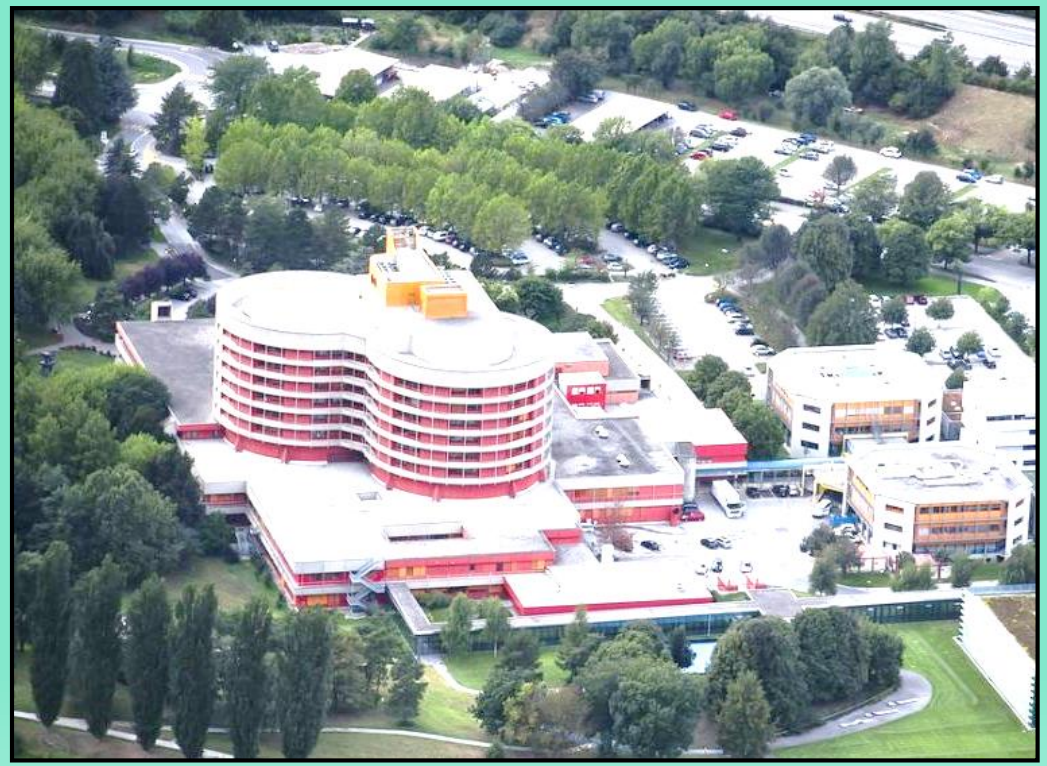
13 maggio 2022



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T. Alp Ikizler, Jerrilynn Burrowes, Laura Byham-Gray, Katrina Campbell, Juan Jesus Carrero, Winnie Chan, Denis Fouque, Allon Friedman, Sana Ghaddar, Jordi Goldstein-Fuchs, George Kaysen, Joel Kopple, Daniel Teta, Angela Yee-Moon Wang, and Lilian Cuppari

Am J Kid Dis 2020

Vol 76 | Iss 3 | Suppl 1 | September 2020

- No guidelines on nutrition/CKD since 2000 and 2007
- Statement of ISRNM for Protein-energy wasting in 2013
- KDOQI Nutrition-CKD guideline process started in 2014
- Very rigorous process (defined questions, mainly RCT)
- Potentiel authors applied to NKF, ADA, then selected according to achievements
- CKD all stages
- Searched databases from 1985 to end of 2016
- Limited to controlled trials for intervention questions

Co-Chairs: T. Alp Ikizler, MD & Lillian Cuppari, PhD, dietitian

- **Macronutrients**
  - Laura Byham-Gray, PhD, RDN, FNKF (Chair)
  - Denis Fouque, MD, PhD
  - Winnie Chan, PhD, RD
  - Jerrilynn Burrowes, PhD, RD, CDN
  - Daniel Teta, MD, PhD

- **Micronutrients**
  - Angela Wang, MD, PhD (Chair)
  - Jordi Fuchs, DSc, APN,NP-C,RD
  - Joel Kopple, MD
  - Sana Ghaddar, PhD, RDN
  - Alp Ikizler, MD

- **Electrolytes & other nutrients**
  - Juan Jesus Carrero, PhD Pharm, PhD Med, MBA (Chair)
  - Katrina Campbell, PhD, RD
  - George Kaysen, MD, PhD
  - Allon Friedman, MD, FASN
  - Lilian Cuppari, PhD

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1. **Low protein diets to stop CKD progression**

2. **Recommendations to prevent/treat protein-energy wasting (PEW) in dialysed patients**

3. **Other topics i.e. diagnosis or PEW, vitamins etc…**

Ideal nutrition for CKD patient (non D) ?

- Should slow CKD progression
- Should retard/postpone dialysis need
- Should have a positive impact on long-term prognosis
- Should limit metabolic derangements typical of the uraemic /advanced CKD stage

In advanced CKD, Low Protein Diets (LPD and VLPD) have many benefits: an historical perspective

- Alleviation of the uraemic syndrome (***Beale et al. 1869; Lyon et al. 1931)***
- Protection of glomerulosclerosis – animals (***Brenner et al. 1980)***
- Anti-proteinuric effect (***Aparicio et al. 1990)***
- **Slow GFR decline ?** ***(Klahr et al, 1994, MDRD)***
- Cochrane analysis on hard endpoints – ESRD/death (***Fouque et al. 2001, 2006, 2009)***
- KDOQI Nutrition Guideline 2020, levels of evidence 1A ***(Ikizler TA, et al. 2020)***

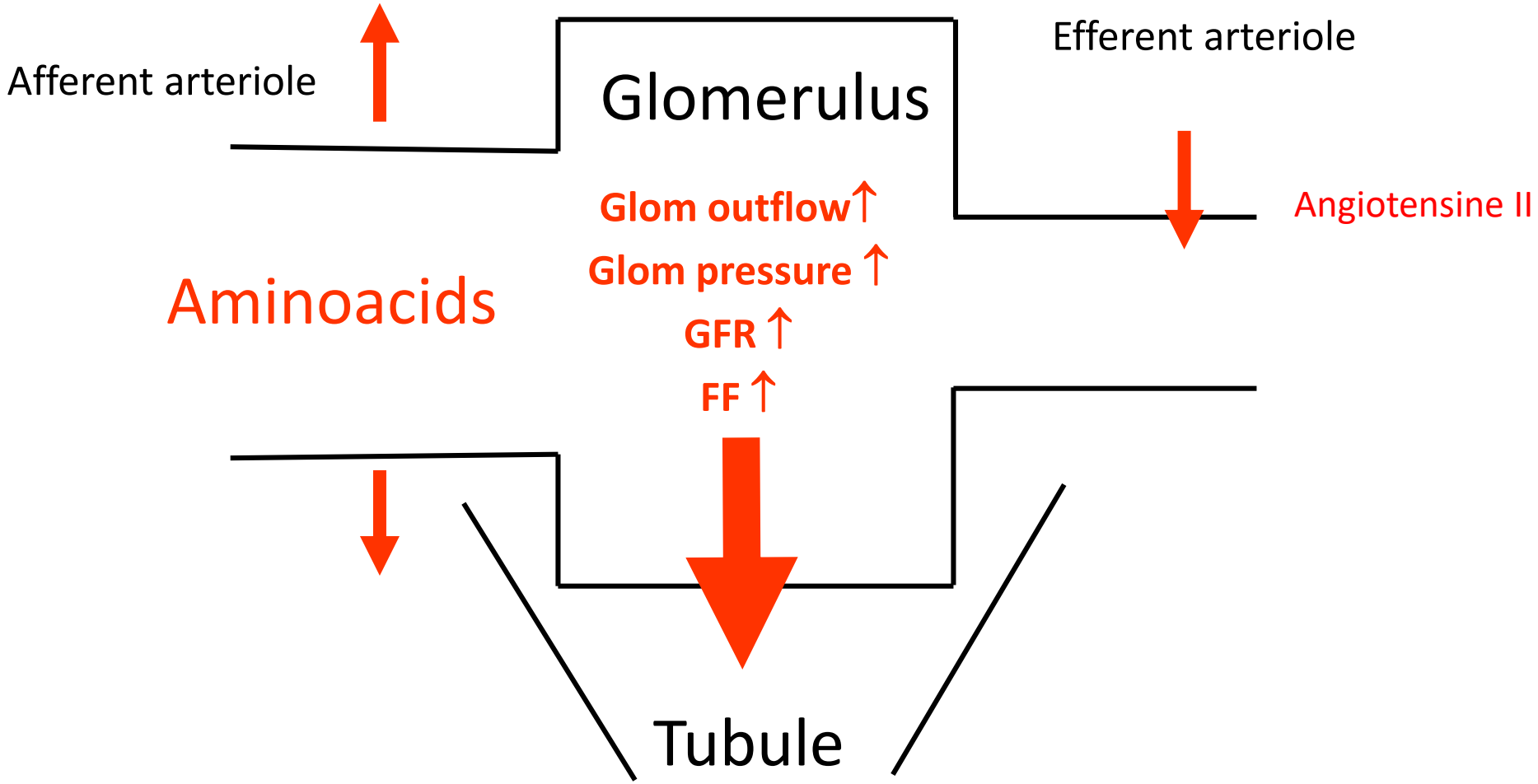
Low protein diet (LPD)

- **LPD: 0.6 – 0.8 g proteins/ideal BW in kg/d**
- NB: Western diet: 1.0-1-5 g/ideal BW in kg/d
- NB: 0.6 -0.8 g proteins/ideal BW in kg/d

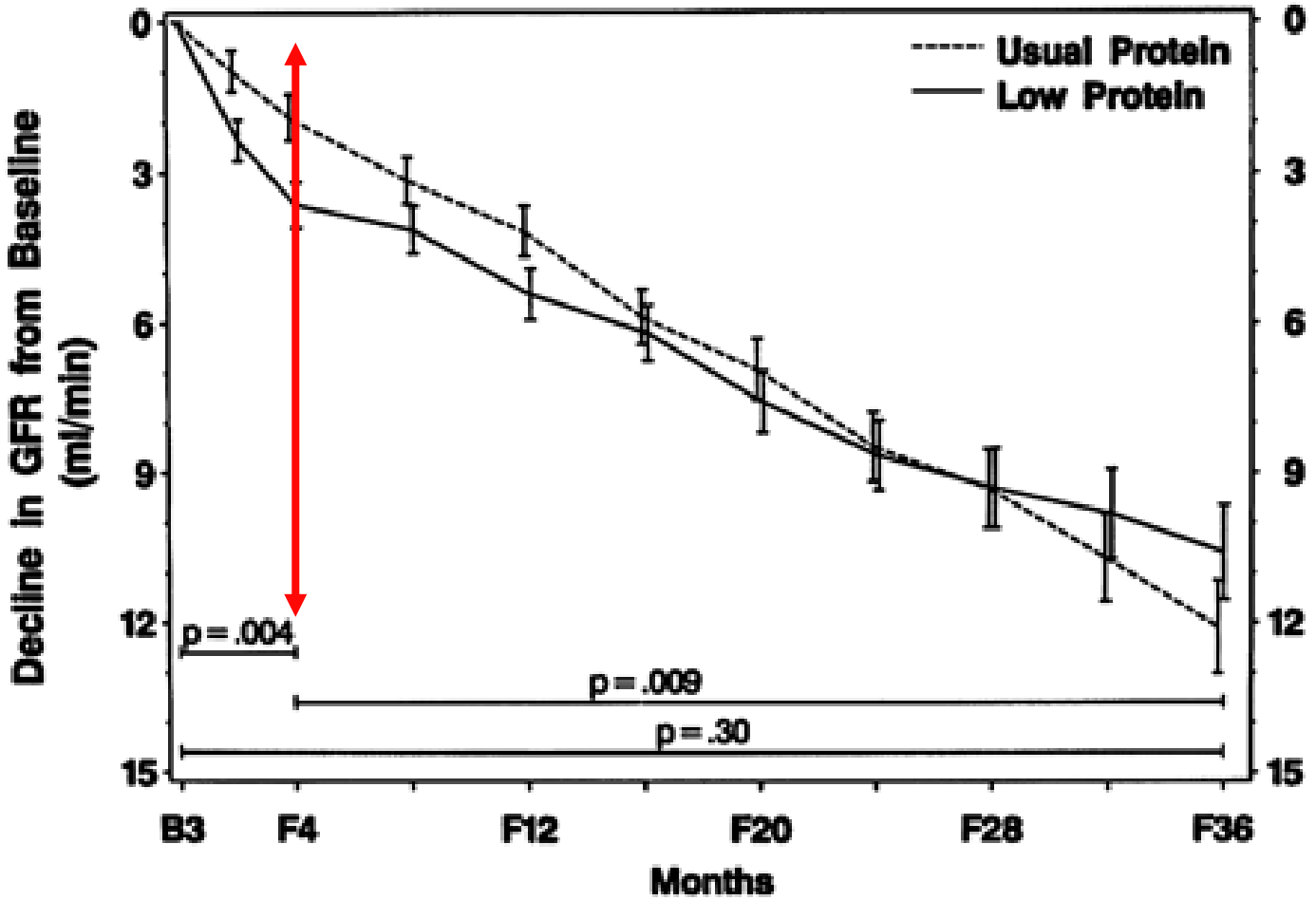
  minimum necessary for a normal individual to maintain a neutral protein balance
- **NB: The Mediterranean/Vegetarian diet use a LPD approach**

Very low protein diet (VLPD) + Ketoacids (KA)

- ✓ **VLPD: 0.3 g Protein/iBW in kg/d**
- ✓ + KA intake is necessary to maintain nitrogen balance in steady state patients
- ✓ The nature of KA (keto-and hydroxy forms of essential amino acids) leads to a greater decrease of serum urea
- ✓ Benefits in proteinuria reduction and in GFR decline are greater than for LPD

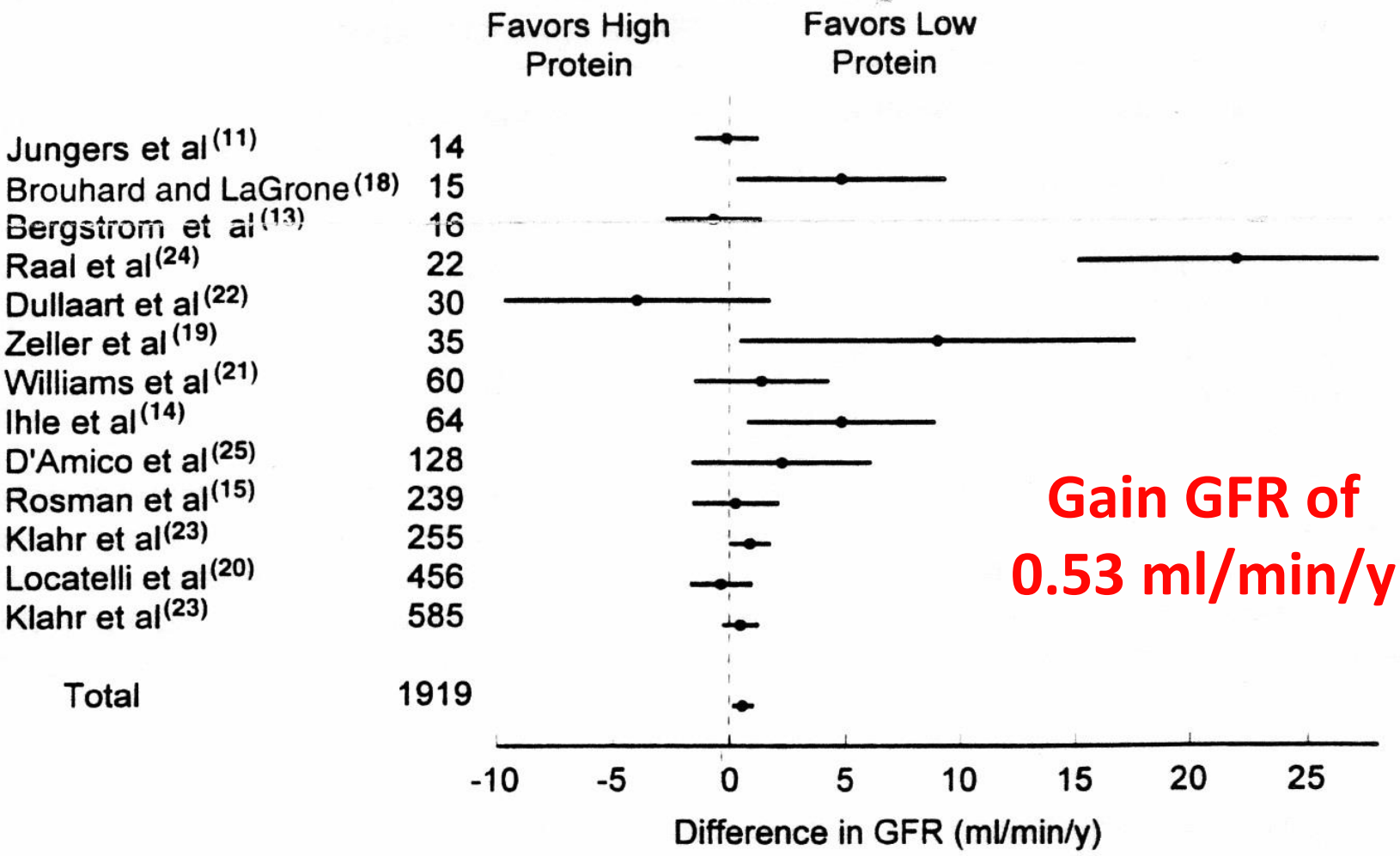

Afferent arteriole
Glomerulus
Efferent arteriole
Angiotensine II
Glom outflow↑
Glom pressure ↑
GFR ↑
FF ↑
Aminoacids
Tubule

MDRD study: 0.6 g/kg/d vs 1.2 g/kg/d



Klahr S et al. New Engl J Med 1994
Levey et al, J Am Soc Nephrol 1999

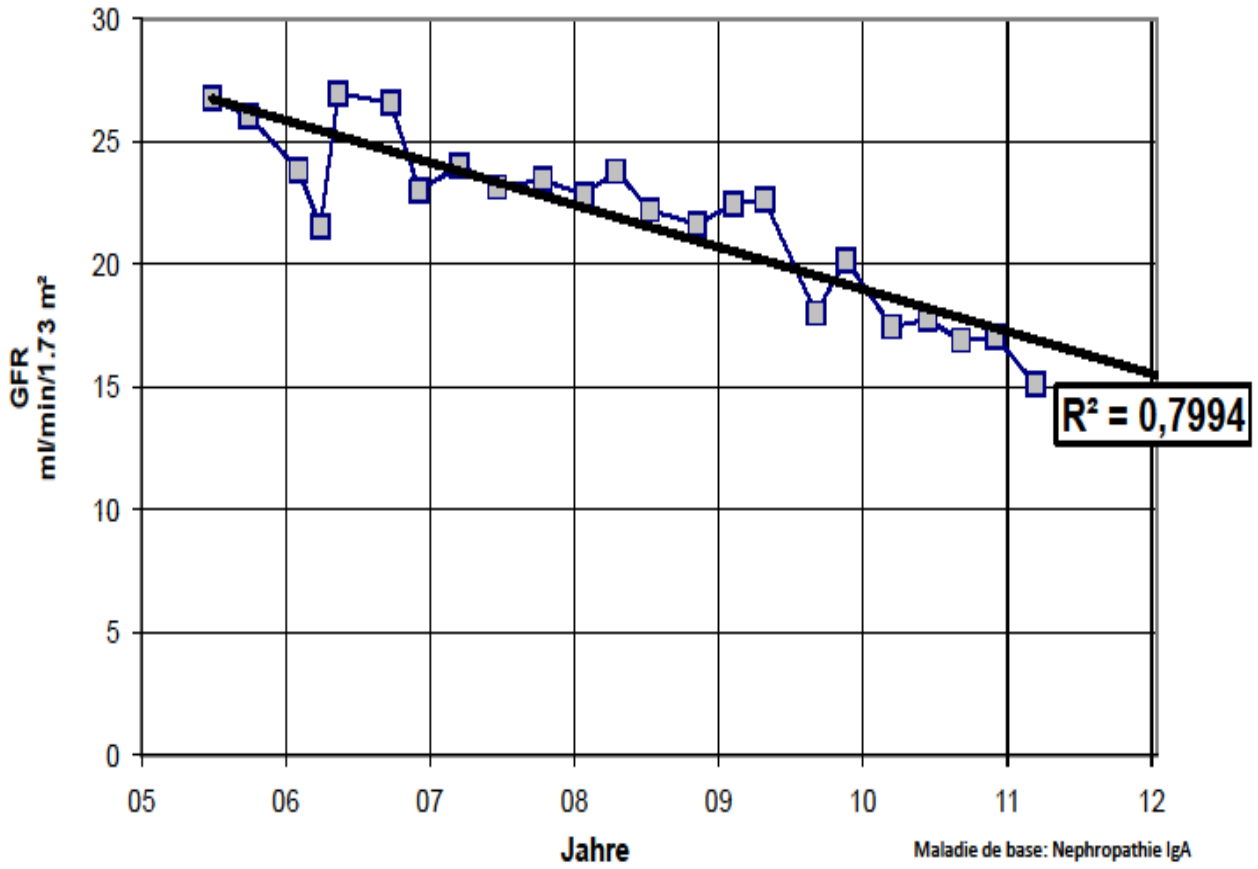
Low protein diet: effect on GFR is small meta-analysis



Gain GFR of 0.53 ml/min/y

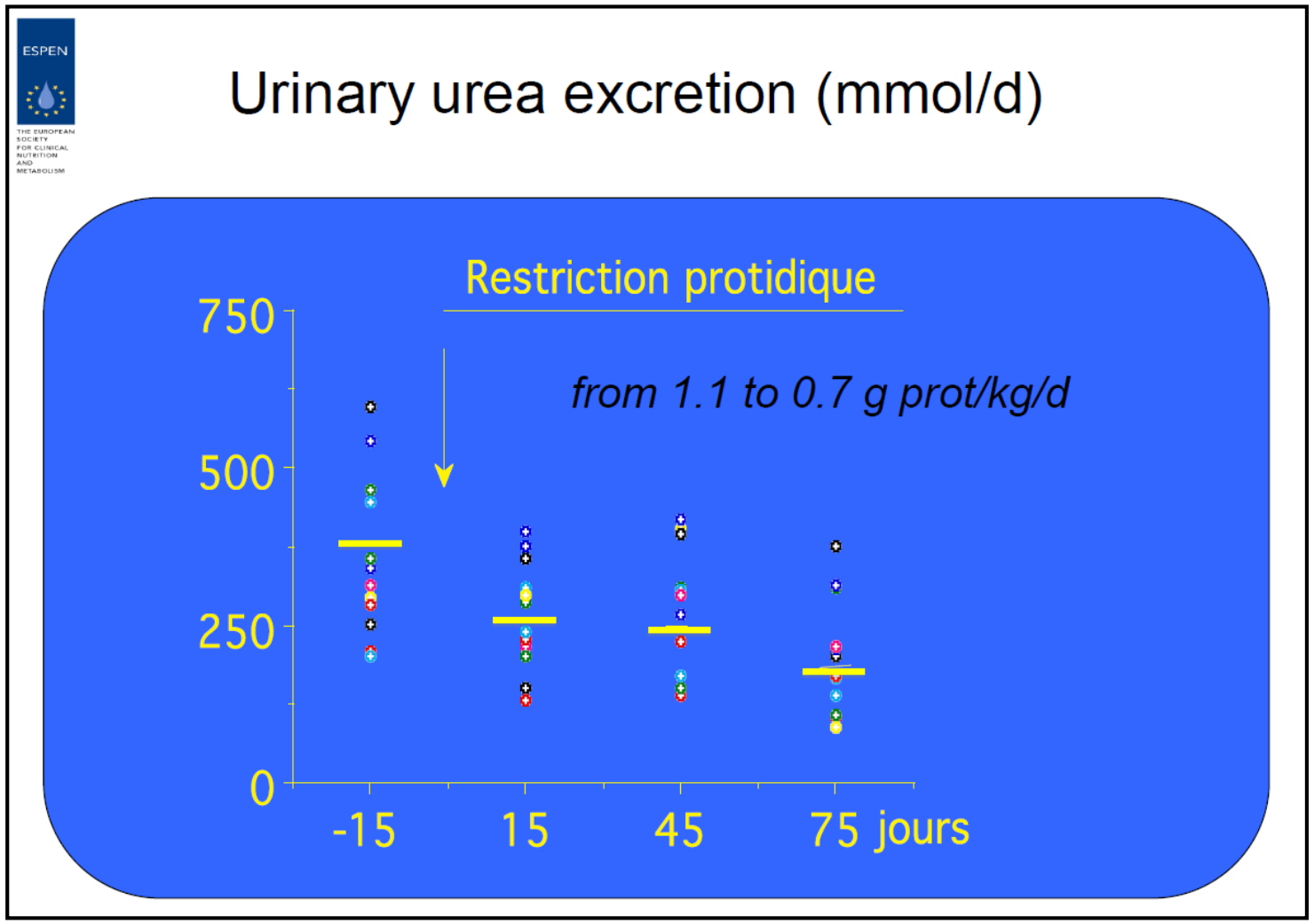
Kasiske et al, Am J Kidney Dis 1998; 31:954-961

Patient 51 years-old (Mr CS)
IgA nephropathy
Low protein diet (LPD)



GFR loss of
1.4 ml/min/1.73 m²

Low protein diet in a CKD patient,
Monitoring of adherence : urinary urea (24h)



Estimation de l'apport protéique journalier

Comment mesure-t-on l'apport protéique d'un patient avec une MRC ?

✓Enquête diététique

✓Récolte urinaire de 24h avec dosage de l'urée urinaire

Apport en protéines

= [excrétion urée urinaire 24h (mmol/L) X 0.18] + 10

Maroni BJ et al. Kidney Int 1985

KDOQI Nutrition guideline 2020
Protein recommendation 1

- **We recommend a low protein diet providing 0.55 to 0.6 g protein/kg per day to:**
  - **reduce the risk for of ESRD/death (1, A)**
  - **maintain QoL (1, C) in adults with stages 3-5 CKD**

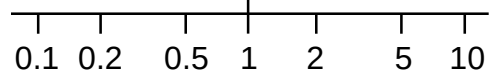
Supporting Evidence: outcomes of interest

- **13 RCTs from 1985 to 2013; 0.55-0.6 vs ≥ 0.8 g protein/kg/d**

  - ESRD/death: beneficial effect of protein restriction (OR 0.62; CI 0.39 to 0.98)
  - QoL: scores for general health and physical status improved significantly after protein restriction
  - Improvement in serum lipid profile
  - NB: Protein restriction had no effect on eGFR
  - NB: Protein restriction had no effect Serum albumin and anthropometrics
  - NB: Uncertain effect on serum phosphate

Low protein diet: effect on renal death is important : meta-analysis

Study or sub-category	Low-protein diet (n/N)	Free/control diet (n/N)	RR (random; 95% CI)	Weight (%)	RR (random; 95% CI)
Di Iorio et al. (2003)[83]	2/10	7/10		2.68	0.29 (0.08–1.05)
Ihle et al. (1989)[79]	4/34	13/38		4.38	0.34 (0.12–0.95)
Jungers et al. (1987)[77]	5/10	7/9		9.02	0.64 (0.32–1.31)
Williams et al. (1991)[78]	12/33	11/32		10.54	1.06 (0.55–2.04)
Klahr et al. (1994)[81]	18/291	27/294		13.85	0.67 (0.38–1.20)
Locatelli et al. (1991)[80]	21/230	32/226		16.95	0.64 (0.38–1.08)
Malvy et al. (1999)[82]	11/25	17/25		17.04	0.65 (0.39–1.09)
Rosman et al. (1989)[76]	30/130	34/117		25.54	0.79 (0.52–1.21)
Total (95% CI)	**763**	**751**		**100.00**	**0.69 (0.55–0.85)**



Favours low-protein diet **Favours free/control diet**

Total events: 103 (low-protein diet), 148 (free/control diet)
Test for heterogeneity: $\chi^2 = 5.78$, df = 7 (p=0.57), F =0%
Test for overall effect: Z = 3.45 (p=0.0006)

N=1514 non diabetic CKD patients:

Reduction of renal death of 31%

Fouque D, Aparicio M. Nat Clin Pract Neprol 2007;3:383–92

THE COCHRANE COLLABORATION®

Low protein diets for chronic renal failure in non diabetic adults (Review)

Fouque D, Wang PH, Laville M, Boissel JP

This record should be cited as:
Fouque D, Wang PH, Laville M, Boissel JP. Low protein diets for chronic renal failure in non diabetic adults. *The Cochrane Database of Systematic Reviews* 2000, Issue 4. Art. No.: CD001892. DOI: 10.1002/14651858.CD001892.

This version first published online: 23 October 2000 in Issue 4, 2000.
Date of most recent substantive amendment: 22 August 2000

Key message

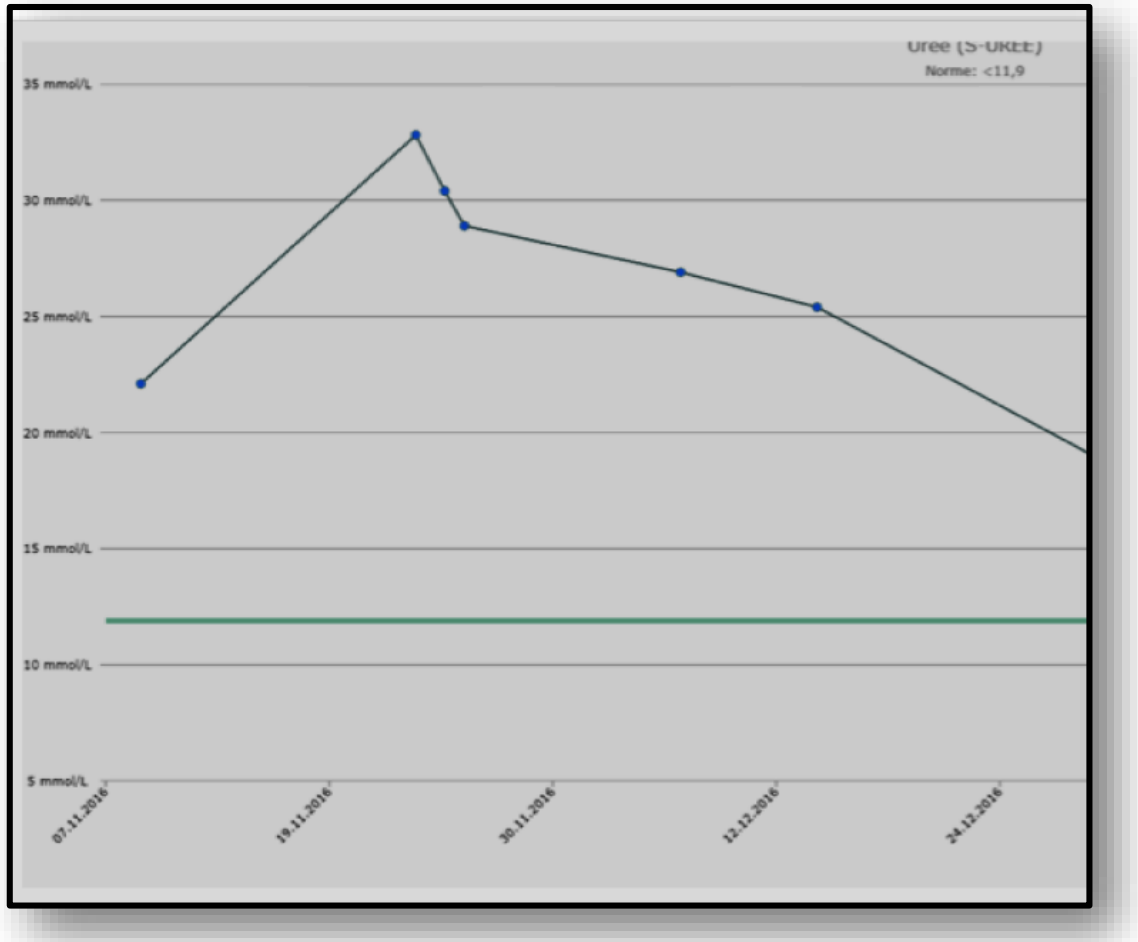
- LPD works well beyond the effect on GFR
- It maintains the CKD patient in a good nutritional/ metabolic health and with no uremic symptoms

This is how LPD delays dialysis start substantially

Very low protein diet (VLPD) + Ketoacids (KA)

- ✓ **VLPD: 0.3 g Protein/iBW in kg/d**
- ✓ + KA intake is necessary to maintain nitrogen balance in steady state patients
- ✓ The nature of KA (keto-and hydroxy forms of essential amino acids) leads to a greater decrease of serum urea
- ✓ Benefits in proteinuria reduction and in GFR decline are greater than for LPD

Very low protein diet (VLPD) in a CKD patient, effect on serum urea



- **Female, 66 years-old polycystic kidney disease**
  Very low protein diet (sVLPD)
  + KA
  + Aproteic food

KDOQI Nutrition guideline 2020
Protein recommendation 2

- **We recommend a very-low protein diet (0.28 to 0.43g protein/ kg per day) supplemented with ketoanalogs (to meet protein requirements)**

  - to reduce the risk of ESRD in adults stages 3-5 CKD (1, B)

Supporting Evidence: outcomes of interest

14 studies (1987 to 2016): 0.3-0.4 g prot/kg/d + KA vs ≥ 0.58 g prot/kg/day

- 2 newer studies show positive effects of VLPD + KA on CKD progression and ESRD (RR 0.42, CI 0.22 to 0.78), (evidence from older studies was unclear effect on ESRD)
- Could help preserve renal function in stage 3 to 5 CKD (1 study in PD also indicated that eGFR was preserved)
- Could decrease S phosphate and improve markers of bone metabolism (calcium, PTH)
- Had no significant effect on S albumin and nutritional status (SGA-anthropometrics)
- Effect on BP inconclusive
- Could improve lipid profile

JASN JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Ketoanalogue-Supplemented Vegetarian Very Low-Protein Diet and CKD Progression

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Received for publication April 8, 2015.
Accepted for publication September 24, 2015.

Abstract

Dietary protein restriction may improve determinants of CKD progression. However, the extent of improvement and effect of ketoanalogue supplementation are unclear. We conducted a prospective, randomized, controlled trial of safety and efficacy of

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This Article

Published online before print January 28, 2016, doi: 10.1681/ASN.2015040369
JASN July 2016 vol. 27 no. 7 2164-2176

Abstract *Free*
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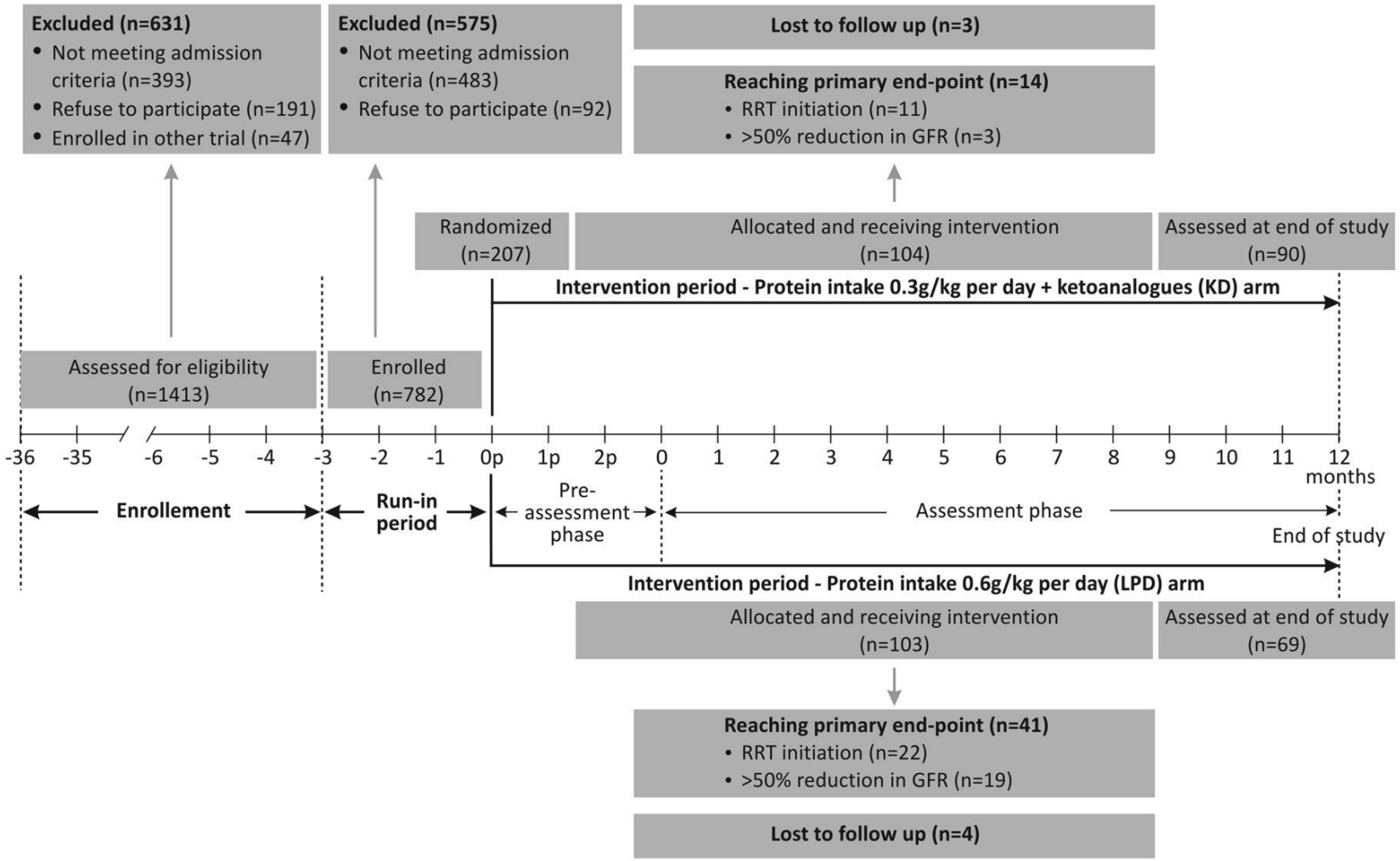
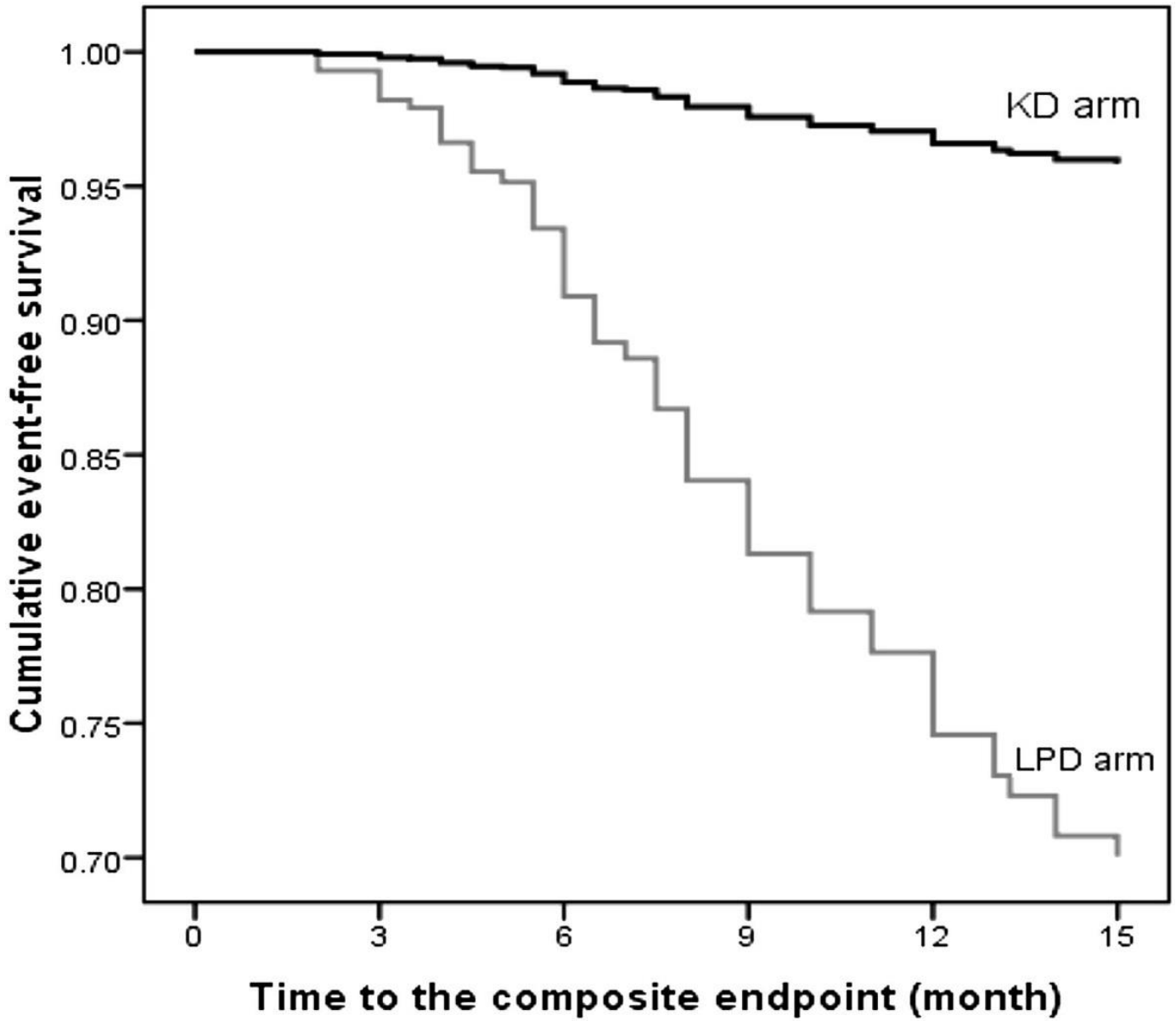
2016

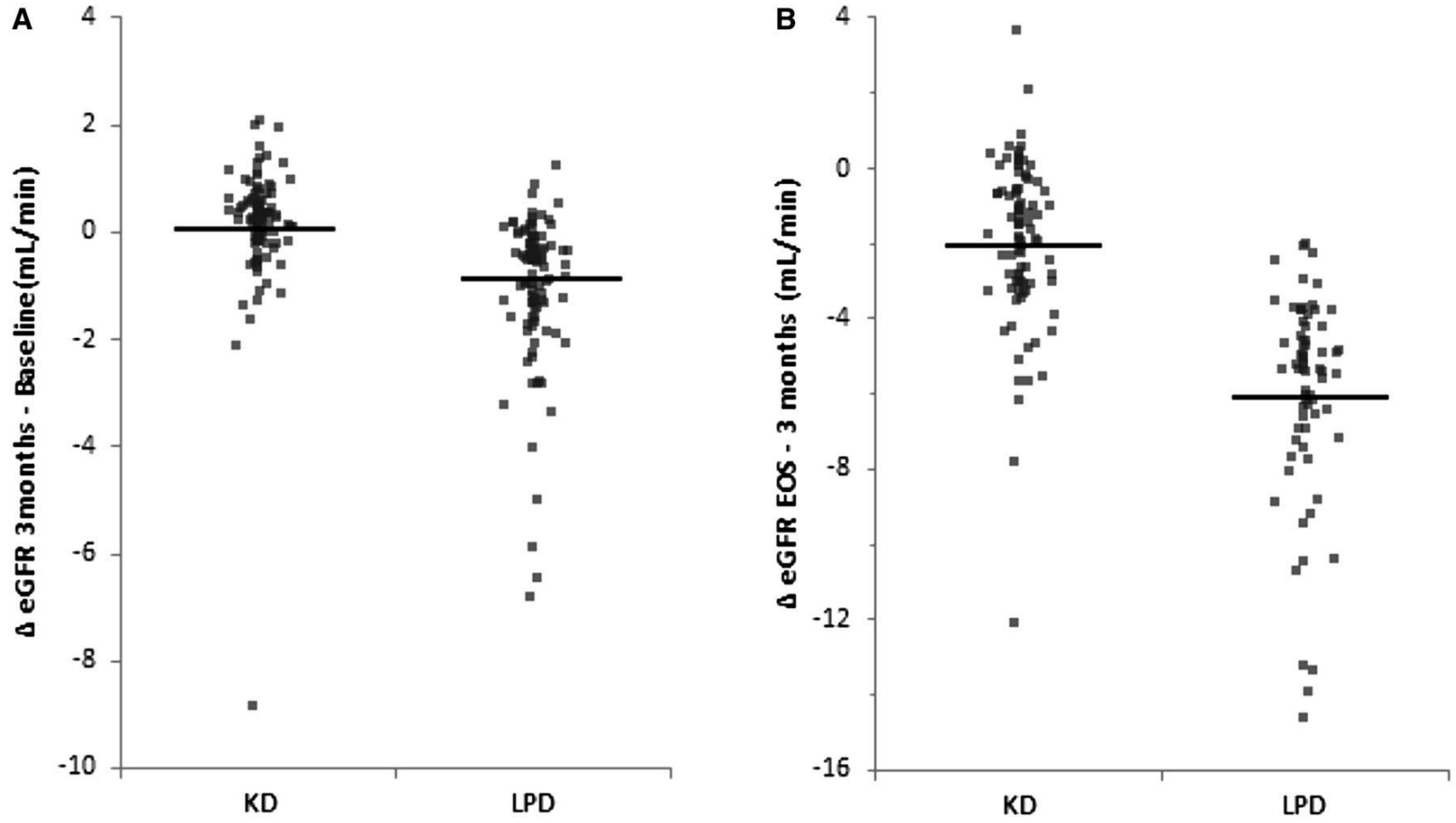
Patients' flowchart.



Liliana Garneata et al. JASN 2016;27:2164-2176

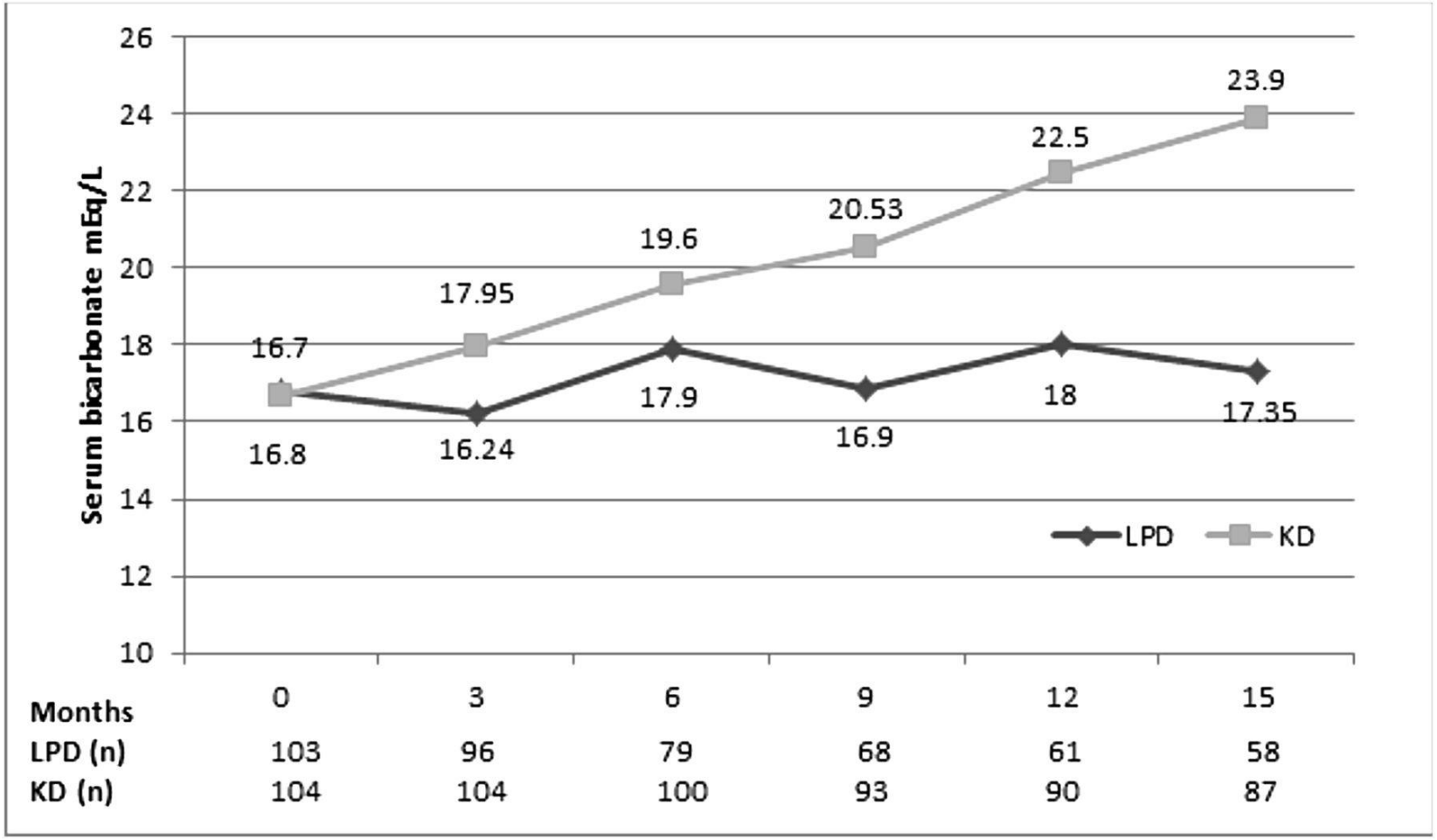

1.00
0.95
0.90
0.85
0.80
0.75
0.70
Cumulative event-free survival
KD arm
LPD arm
0
3
6
9
12
15
Time to the composite endpoint (month)

Median changes in eGFR (95% CI) between study moments (Δ implies statistically significant difference between the two groups).



Liliana Garneata et al. JASN 2016;27:2164-2176

Serum bicarbonate (milliequivalents per liter) during the study.

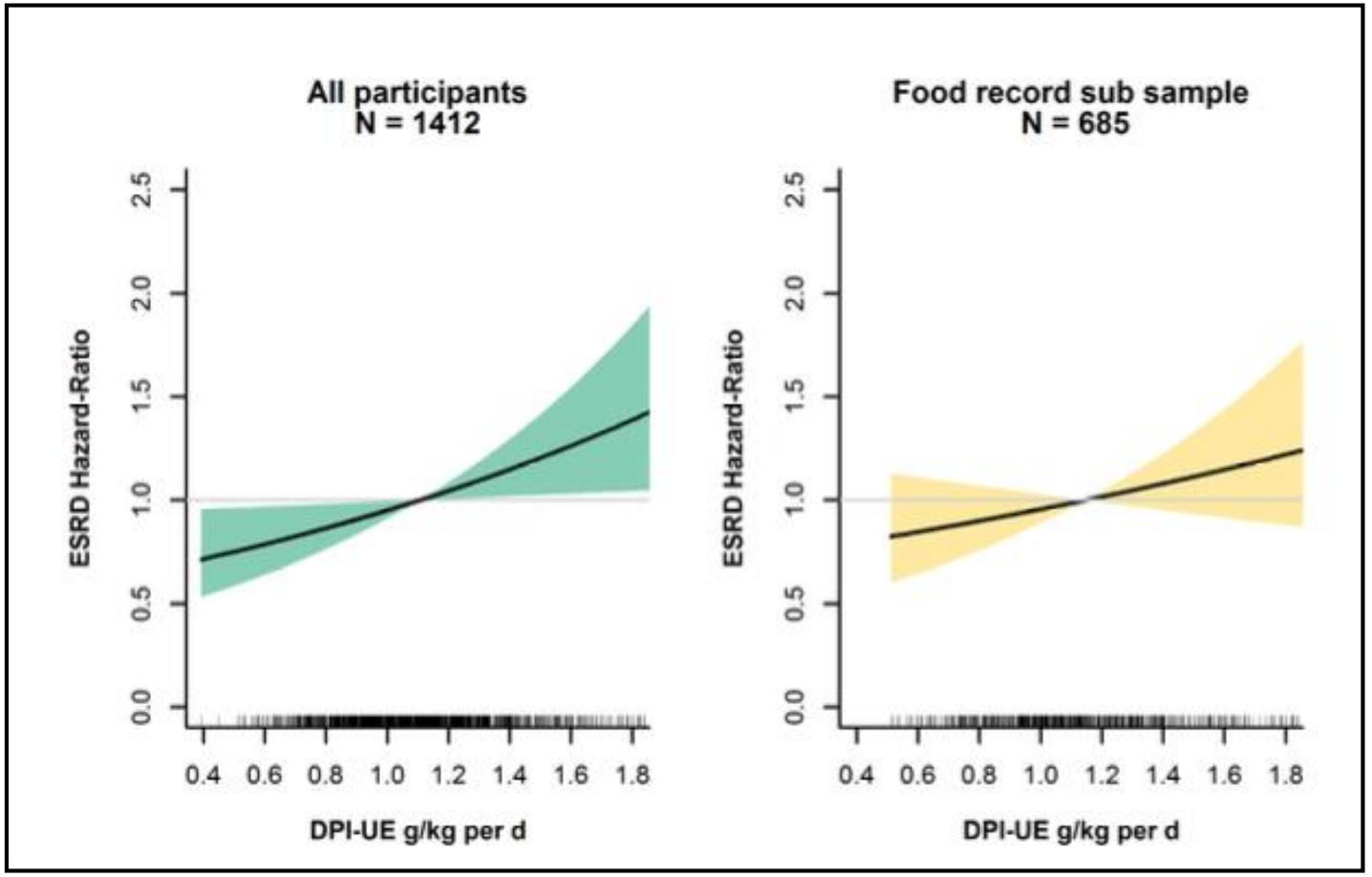


Liliana Garneata et al. JASN 2016;27:2164-2176

Key Message

- **If CKD patients are motivated to adhere sVLPD, this is a powerful wheapon to tackle CKD progression**

CKD KILLER



Nephrotest Paris

1412 CKD3 patients
3.5 yr survival

Metzger et al.
Kidney Int Rep. 2017;3:105-114

Typical claim of opponents of LPD
« LPD leads to malnutrition»

Do LPD sVLP lead to malnutrition / PEW ?

1. MDRD study:

   → Only 2 patients /255 in LPD group dropped out of the study due to malnutrition !

2. MDRD study: 9 months after the end of the study

   - Low protein diet group: Albumin: 42 ± 4 g/L ***(Menon V, et al. AJKD 2009)***

   - Very low protein diet group: Albumin: 42 ± 5 g/L

3. Studies in Bordeaux: 239 patients followed at long term:
   no PEW/malnutrition, maintain of body composition

Aparicio M, et al. J Am Soc Nephrol 2000
Chauveau P, Am J Kid Dis 1999 and J Ren Nutr 2003

Key message

LPD and sVLPD do not lead to malnutrition but,
if LPD – sVLPD are applied correctly

<u>4 conditions to be met:</u>

a) Energy intake: 30-35 kcal/kg/day

b) Serial nutritional assessments and follow-up by trained dietitians

c) Do not apply if malnutrition/PEW

d) Stop if occurrence of catabolic event (hospitalisation)

Conclusions, CKD 3-5

- LPD and sVLPD mainly work through prevention of dialysis start
- To be implemented with specialized renal dietitians
- Monitor nutritional status and compliance

Implementation of KDOQI Nutrition Guidelines 2020

- Convince nephrologists and train them to low protein diets
- Increase the training and number of **specialized renal dietitians** in hospitals/clinics
- Promote **low protein products** to simplify dietary counseling and help achieving low protein diet
- Enforce the dietary interventions to improve symptoms **when chronic dialysis is not a treatment option or is to be postponed** (vascular access maturation, organizing pre-emptive renal transplant, ..)

Implementation of KDOQI Guidelines - monitoring

- Compliance to diets should be monitored frequently during the first year of dietary intervention by dietary interviews (4-6 are optimal) and urine collection for urea output measures.

- Then yearly follow-up recommended

Dietiste per favore !!!