

Implementing Nutritional and Dietary Management of CKD under the US President's Executive Order

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Editor-in-Chief
Journal of Renal Nutrition (JREN)



Disclosure of Financial Relationships

Kamyar Kalantar-Zadeh, MD, MPH, PhD

Dr. K. Kalantar-Zadeh has received honoraria and/or support in different forms from Abbott, Abbvie, Alexion, Amgen, ASN (American Society of Nephrology), Astra-Zeneca, Aveo, Chugai, DaVita, Dr. Schaer, Fresenius, Genentech, Haymarket Media, Hofstra Medical School, IFKF (International Federation of Kidney Foundations), ISH (International Society of Hemodialysis), International Society of Renal Nutrition & Metabolism (ISRNM), JSDT (Japanese Society of Dialysis Therapy), Hospira, Kabi, Keryx, Novartis, NIH (National Institutes of Health), NKF (National Kidney Foundations), Pfizer, Relypsa, Reata, Resverlogix, Sandoz, Sanofi, Shire, US Renal Care, Vifor, UpToDate, ZS-Pharma.

Nutritional and Dietary Management of Kidney Disease: A Patient Care Approach

- **We are what we eat: Learn how to enforce kidney health through nutrition and diet**
- **Saturday, Feb. 29, 2020 – 7:30 am - 4:45 pm**
- **University of California Irvine (UCI) Medical Center, Bldg. 53, Auditorium 101**
- **The City Drive South, Orange, California 92868, USA**
- **UCI Nephrology has teamed up with the nation's leading experts to leverage their interests and expertise to provide insights on real-world clinical management and hands-on workshops for dietary approaches.**
- This is a full-day CME course for physicians (nephrologists, internists, urologists and family practitioners) and other healthcare providers and allied health professionals (dietitians, nurses, nutritionists and researchers) who will learn the pathophysiology and mechanisms related to the role of nutrition in kidney disease and kidney health.

SAVE THE DATE

UCI Health

Nutritional and Dietary Management of Kidney Disease: A Patient Care Approach

We Are What We Eat: Learn How to Enforce Kidney Health through Nutrition and Diet

Saturday, February 29, 2020
7:30 a.m. to 4:45 p.m.

UCI Nephrology has teamed up with the nation's leading experts to leverage their interests and expertise to provide insights on real-world clinical management and hands-on workshops for dietary approaches.

UCI Health Medical Center
Bldg. 53, Auditorium
101 The City Drive South
Orange, CA 92868

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For more information:
Krzysztof Fuentebella at kfuente@uci.edu | 714-456-5142



- 7:00-7:30 AM: Registration begins & Event/Exhibitor Setup
 7:30-8:00 AM: Registration, Breakfast & Exhibitors
 8-8:30 AM: **Introduction & Lecture 1: Nutrition in non-dialysis-CKD in the Era of Executive Order to Prevent ESRD (Dr. Kamyar Kalantar-Zadeh, 25+5 min)**
 8:40-9:20 AM: Lecture 2: **Dietary Plant-Based Approaches to Kidney Disease** (Dr. Sean Hashmi, 25+5 min)
 9:20-9:50 AM: Lecture 3: **Nutritional Management of Diabetic Kidney Disease** (Dr. Connie Rhee, 25+5 min)
 9:50-10:10 AM: AM Break & Exhibitors (20 min)
 10:10-10:40 AM: Lecture 4: **Nutritional Disorders in Children with CKD: Evaluation and Therapeutic Options** (Dr. Robert Mak, 25+5 min)
 10:40-11:10 AM: Lecture 5: **Microbiome, Prebiotics, Probiotics** (Dr. Wei Ling Lau, 25+5 min)
 11:10-11:50 AM: Lecture 6: **Metabolic Evaluation and Medical Treatment of Urolithiasis: "Stone Trees"** (Dr. Ralph Clayman, 25+5 min)
 11:50-12:20 AM: **Lecture 7: Complementary and Integrative medicine for CKD** (Dr. Arvin Jenab, 25+5 min)
 12:20-1:20 PM: **Workshop with working lunch:**
 1. Case 1: Calculating dietary intake adherence using 24-hour urine (Dr K. Kalantar 10+5 min)
 2. Case 2: Suggested meal plans for ND-CKD and transplanted patients (Ms. Meghan Donnelly, 10+5 min)
 3. Case 3: Working more effectively with dietitians (Dr Joel Kopple, 10+5 min)
 1:20-2:00 PM: Lecture 8: **Nutritional Management of AKI** (Dr. Etienne Macedo, 25+5 min)
 2:00-2:40 PM: Lecture 9: **Keto-analogues and Very Low Protein Diet in CKD and Advanced Uremia** (Dr. Joel Kopple)
 2:40-3:10 PM: Lecture 10: **Nutrition in Solitary Kidney Care and Kidney Transplantation** (Dr. Ekamol Tantisattamo)
 3:10-3:30 PM Break & Exhibitors (20 min)
 3:30-4:00 PM: Lecture 11: **Nutrition in dialysis and IDPN** (Dr. Kalantar-Zadeh, 25+5 min)
 4:00-4:30 PM: Lecture 12: **Phosphorus, potassium and acid/base in CKD and ESRD** (Dr. Rhee, 25+5 min)
 4:30-4:45 PM: Wrap up and take-home messages

120,000 Americans TRANSITION to Dialysis Each Year Nearly half of them are diabetics

Historical Background:

In 1972 the US Congress extended Medicare coverage to all persons under age 65 suffering from ESRD (End-Stage Renal Disease), i.e. individuals who cannot survive without kidney dialysis treatment, to cover all costs related to their dialysis Rx.

The intent of this law (PL 92-603, the Social Security Amendments of 1972) was to allow all Americans access to an emerging and very expensive technology, regardless of their ability to pay.



The effectiveness of the ESRD program:

No Kidney Function = No Life → **Hope**

→ Dialysis = Life (?)

July 10, 2019: USA President's Executive Order "The Advancing American Kidney Health Initiative"

The Advancing American Kidney Health Initiative:

1. Reduce the number of Americans developing ESRD by 25% by 2030
2. Aim for 80% of new American ESRD patients in 2025 receiving either home dialysis or a transplant
3. Aim to double the number of kidneys available for transplant by 2030

Increase Access
to Kidney
Transplants

Reduce the Risk
of Kidney
Failure

Improve Access to
Treatment
Options for
Kidney Failure





The Advancing American Kidney Health Initiative Payment Models

- 5 CMMI payment models
- 4 optional, 1 mandatory (ERSD Treatment Choices (ETC) Model)
- ETC Model published as proposed rule on July 10



GOALS

- Increase transplant (kidney and kidney-pancreas) and home dialysis rate across the country
- Better manage CKD 4 and 5 patients' transition to dialysis: promote later and better dialysis starts

EDITORIAL

JREN, September 2019 issue

Implementing the “Advancing American Kidney Health Initiative” by Leveraging Nutritional and Dietary Management of Kidney Patients



Linda W. Moore, PhD, RDN
Houston Methodist Hospital, Houston, TX

Kanyar Kalantar-Zadeh, MD, MPH, PhD
University of California Irvine, Irvine, California

THIS MONTH'S EDITORIAL of the *Journal of Renal Nutrition* (JREN) is devoted to both the recent presidential Executive Order (EO) on kidney health initiatives and the articles published in this issue of JREN. On July 10, 2019, the US government took a series of actions to advance kidney care in the nation including a presidential EO entitled, “Advancing American Kidney Health Initiative.”¹ The EO's intention is to prevent kidney failure

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On July 10, 2019, the US government took a series of actions to advance kidney care in the nation including a presidential EO entitled, “Advancing American Kidney Health Initiative.” The EO's intention is to prevent kidney failure through better diagnosis and treatment as well as better incentives for preventative kidney care. To achieve the goal of transforming chronic kidney disease (CKD) prevention and management and to better increase education and awareness to this end, 3 broad goals are proposed for delivering the new policies:

- (1) reducing the number of Americans developing end-stage renal disease (ESRD) by 25% by 2030 through improved efforts to prevent, detect, and slow the progression of kidney disease;
- (2) aim for 80% of new American ESRD patients receiving dialysis in the home or receiving a transplant by 2025;
- (3) (Aim to double the number of kidneys available for transplant by 2030.

Moore & Kalantar-Zadeh, J Ren Nutr, Sep 2019

EDITORIAL

Implementing the "Advancing American Kidney Health Initiative" by Leveraging Nutritional and Dietary Management of Kidney Patients

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nutritional interventions play a critical role and should be reinforced." Nutritional interventions are also important strategies for the primary prevention of kidney disease, given that obesity, diabetes, and hypertension, the 3 main risk factors of chronic kidney disease (CKD), are amenable to nutritional and dietary interventions." Emerging data suggest that Americans eat increasingly more protein (1.3-1.8 g/kg/day) than the Rec-



Nutritional Intervention for the AAKHI in 2020-2030

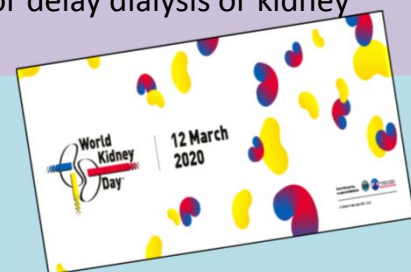
- The Renal Nutrition community enthusiastically welcomes this timely US Government Executive Order (EO) and reminds the government and all stakeholders that in the midst of these positive developments, it is important to reiterate the critical role of nutritional and dietary interventions to achieve and enhance these goals in persons with or at risk for kidney disease. As discussed in our previous commentaries,[2-4] under the context of **secondary prevention** in persons with earlier signs of CKD including microalbuminuria or renal hyperfiltration, for both persons with native kidneys and kidney transplant recipients, eating **low-sodium** (.2.3 g/ day) and **low-protein** (0.6-0.8 g/kg/day) foods should be the cornerstone of nonpharmacologic approaches. These measures can also result in slowing CKD progression and avoiding or delaying ESRD transition.[5]
- For the **tertiary prevention of CKD**, i.e., improving patient longevity and managing comorbidities in those with advanced CKD, nutritional interventions play a critical role and should be reinforced.[6,7]

Moore & Kalantar-Zadeh, *J Ren Nutr*, Sep 2019

Primary/Secondary/Tertiary Prevention of CKD

- **Primary Prevention:** Focus on the modification of risk factors and addressing structural abnormalities of the kidney and urinary tracts, as well as exposure to environmental risk factors and nephrotoxins.
- **Secondary Prevention:** In persons with pre-existing kidney disease ... blood pressure optimization, glycemic control, **dietary modifications** should be the main goal of education and clinical interventions.
- **Tertiary Prevention:** In patients with advanced CKD, management of co-morbidities such as uremia and cardiovascular disease ... to avoid or delay dialysis or kidney transplantation.

Li ... Kalantar-Zadeh, for the World Kidney Day Steering Committee. Kidney Health for Everyone Everywhere - from **Prevention** to Detection and Equitable Access to Care. **World Kidney Day, March 12, 2020** (to be published in >50 journals)



Lifestyle Modification

- Lifestyle modification involves altering habits, typically of eating and physical activity, to maintain health and prevent disease. Lifestyle modification is a key component of the management of Diabetes, CKD and DKD.

- Lifestyle Modification**
- (1) Nutrition & Diet
 - (2) Physical Activity
 - (3) psychosocial care
 - (4) Smoking cessation
 - (5) diabetes self-management education & support

Lifestyle Modification	Diabetes	CKD	DKD
Nutrition & Diet: Eat healthy	Yes	Yes	Same as CKD?
Physical Activity: Exercise	Yes	?	?
psychosocial care: Manage stress, Hope	Yes	Yes?	Same as CKD
Smoking cessation & Watch your alcohol	Yes	No?	?
self-management education & support	Yes	Yes?	Same as CKD

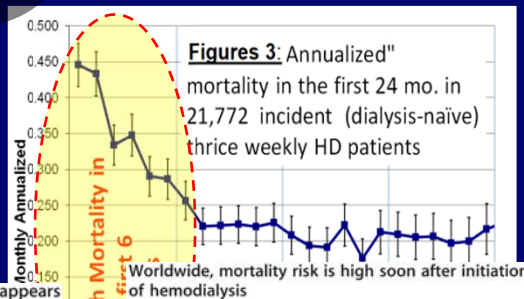


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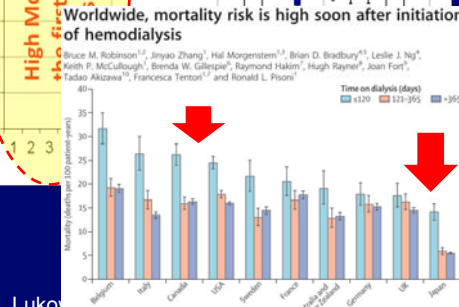
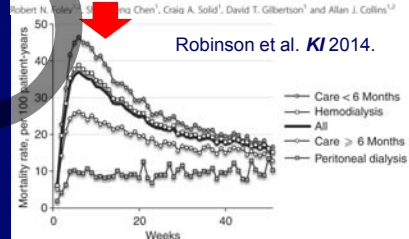
Challenges of Transition to Dialysis:

Very High Early Mortality after Transition

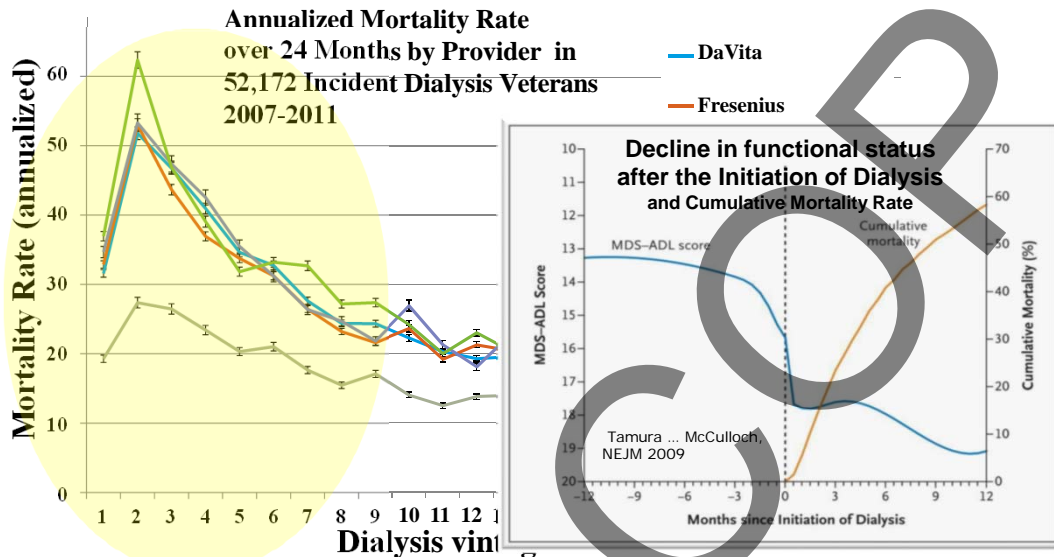
The first 3-6 months of dialysis is associated with an even higher risk of death compared to prevalent dialysis patients.



Early mortality in patients starting dialysis appears to go unregistered



Challenges of Transition from NDD-CKD to ESRD: Higher mortality and worse functional after transition to dialysis



[USRDS Transition of Care in CKD, Veterans Data, www.USRDS.org](http://www.USRDS.org)

Transition of Care from CKD to ESRD

It is not clear whether the poor outcomes of RRT justify these expensive therapies in esp. if mortality remains essentially unchanged

**CONSRVATIVE & PRESERVATIVE
MANAGEMENT of CKD
Dialysis Freedom**

RRT: kidney replacement therapy

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~~Elderly Patient's Choice:~~

What would be your preference if you had [Advanced] CKD with or without diabetes?

1. To start dialysis therapy as soon as possible
 2. To start dialysis therapy as soon as possible
 3. To start dialysis therapy as soon as possible
- CONSERVATIVE and PRESERVATIVE MANAGEMENT of CKD:**
- To avoid dialysis, later dialysis, less dialysis**
1. Slow CKD progression rate by dietary interventions
 2. Manage uremia without dialysis by dietary interventions
 3. Improve longevity and functionality without dialysis.

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Part 6

High Protein Diet (LPD)

VS.

Low Protein Diet (LPD)

in DKD

Barriers to Low Protein Diet Therapy for the Management of CKD

Challenge 1:

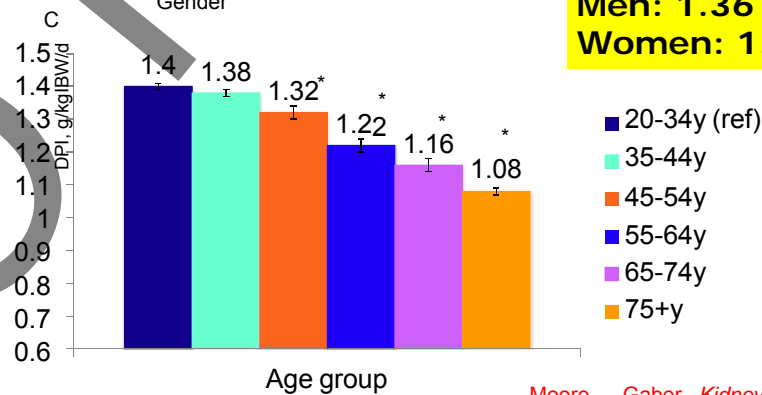
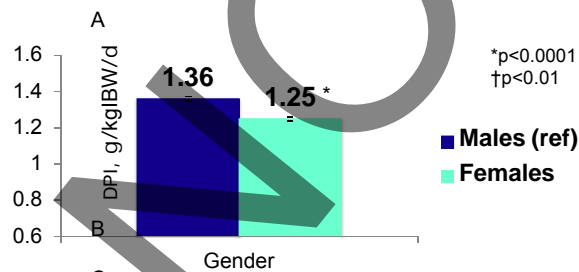
Developed nations eat HIGH PROTEIN Diet!

"High protein diet makes you thin!?"

- We need to provide consistent education for avoiding high protein diet!



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NHANES data:

How much protein do people of different ages eat in the USA?

Men: 1.36 g/kg/d

Women: 1.25 g/kg/d

Moore ... Gaber. *Kidney Int* 2013

What is a Low and Very Low Protein Diet

- To slow the rate of kidney failure progression over time
- To mitigate and/or control uremia:

1. How low? :

1.2 g/kg/day → 1.0 → 0.8 → 0.6 → 0.5 →

2. With or without keto- or amino-

3. Risk of malnutrition

- To Answer these questions, the MDRD Study was performed from 1994

KDOQI Renal Nutrition 2020 will recommend
0.55-0.60 g/kg/day for non-diabetic NDD-CKD
and 0.8 to 0.9 for diabetic CKD (DKD)

Barriers to Low Protein Diet Therapy for the Management of CKD in the Elderly

Challenge 2:

Many nephrologists are trained to believe that MDRD Study was a failure!

“Low Protein Diet has no effect?”

MDRD: Modification of Diet in Renal Disease

**LPD to sVLPD: effect on CKD progression?
MDRD study (CKD stage 3) *NEJM 1994***

Volume 330:877-884 March 31, 1994 Number 13 [Next ▶](#)

The Effects of Dietary Protein Restriction and Blood-Pressure Control on the Progression of Chronic Renal Disease

Saulo Klahr, Andrew S. Levey, Gerald J. Beck, Ariene W. Caggiula, Lawrence Hunsicker, John W. Kusek, Gary Striker, for The Modification of Diet in Renal Disease Study Group

Background Restricting protein intake and controlling hypertension may slow the progression of renal disease in animals. We tested these interventions in 840 patients with chronic renal insufficiency.

Methods In study 1, 585 patients with glomerular filtration rate (GFR) of 13 to 24 ml per minute per 1.73 m² of body-surface area were randomly assigned to a usual-protein diet (1.3 or 0.58 g of protein per kilogram of body weight per day) and to a low-blood-pressure group (mean arterial pressure, 107 or 92 mm Hg). In study 2, 255 patients with a GFR of 13 to 24 ml per minute per 1.73 m² were randomly assigned to the low-protein diet (0.28 g per kilogram per day) or a very-low-protein diet (0.28 g per kilogram per day) with a keto acid supplement, compared with a usual- or a low-blood-pressure group (same values as those in study 1). An 18-month follow-up was planned, with monthly evaluations of the patients.

Conclusions Among patients with moderate renal insufficiency, the slower decline in renal function that started four months after the introduction of a low-protein diet suggests a small benefit of this dietary intervention. Among patients with more severe renal insufficiency, a very-low-protein diet, as compared with a low-protein diet, did not significantly slow the progression of renal disease.



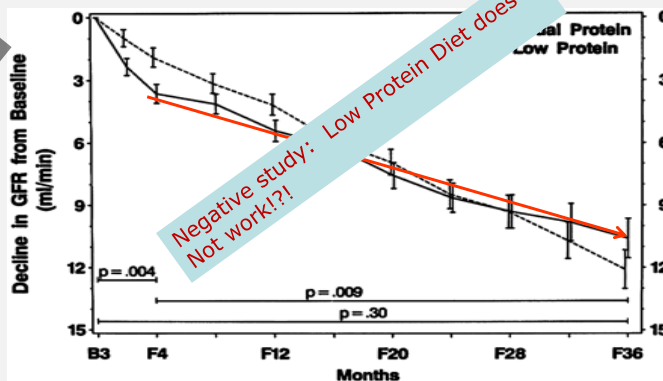
Negative study:
Low Protein Diet
does Not work!?!?

MDRD: Modification of Diet in Renal Disease

MDRD study 1: secondary analysis

Limitations of the MDRD Study

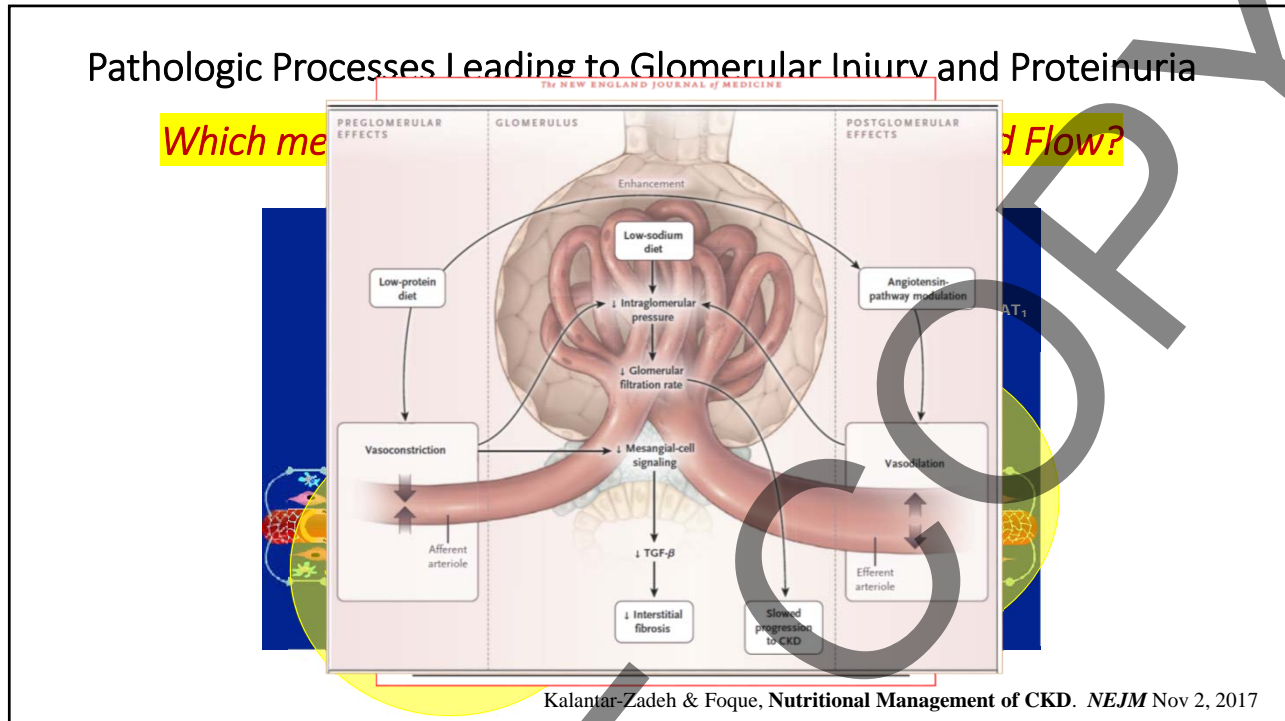
- Small sample size
- Lack of diabetes representation
- Over-representation of polycystic kidney disease
- Relatively short follow-up period
- Failure to separate the temporary short-term versus more persistent long-term effects on GFR
- Discounting secondary analyses
- Discounting post-trial long-term follow-up
- Discounting racial disparities



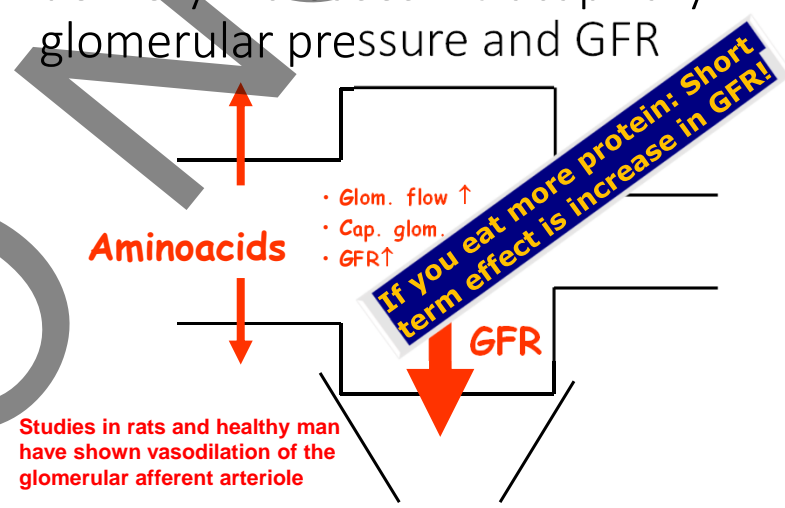
Levey AS et al, J Am Soc Nephrol 1999; 10: 2426-2439

Kalantar-Zadeh & Foque, Nutritional Management of CKD. *N Engl J Med.* 2017

Pathologic Processes Leading to Glomerular Injury and Proteinuria



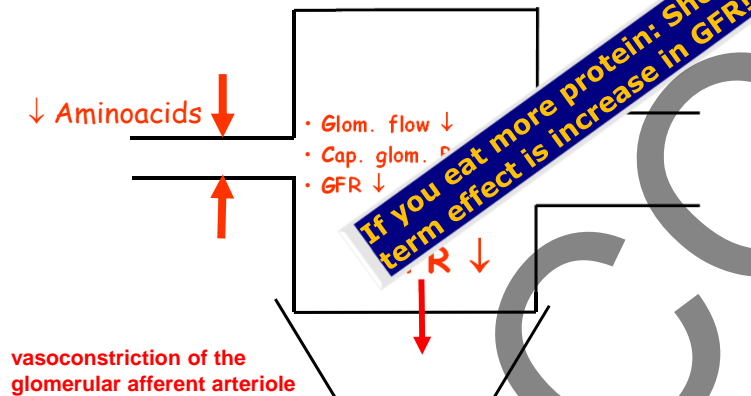
Amino acids (dietary protein intake) delivery increases intracapillary glomerular pressure and GFR



Studies in rats and healthy man have shown vasodilation of the glomerular afferent arteriole

Kalantar-Zadeh & Foque, *Nutritional Management of CKD. NEJM* Nov 2, 2017

Aminoacid (dietary protein intake) restriction decreases intracapillary glomerular pressure and GFR



Kalantar-Zadeh & Foque, Nutritional Management of CKD. *NEJM* Nov 2, 2017

Observational studies about the deleterious effect of high protein diet on renal function

Table 2. Recent observational studies about high-protein diet on renal function

References	Sample size	Mean age (years)	Duration (years)	HP diet	Baseline eGFR (ml/min/1.73 m ²)	Renal function changes
Knight <i>et al.</i> 2003 [11]	1624	55.4	11	Divided into quintiles (fifth group: 93 g/day)	Normal: >80; mild CKD: 55–80	HP was not associated with eGFR decline in normal renal function. However, it was associated with accelerated eGFR decline in mild CKD, particularly with high intake of nondairy animal protein
Halbesma <i>et al.</i> 2009 [12]	8461	49.8	6.4	Divided into quintiles (fifth group: 1.42–3.27 g/kg/day)	Mean 80.6	There was no association of protein intake and rate of eGFR changes
Lin <i>et al.</i> 2011 [15]	3121	67	12	Divided into quartiles (fourth group: 78 g/day)	Median 76	HP was directly associated with microalbuminuria (highest quartile vs. lowest OR, 2.17; 95% CI, 1.18–3.66; <i>P</i> =0.01), and rapid eGFR decline (OR, 1.77; 95% CI, 1.03–3.03)
Dunkler <i>et al.</i> 2013 [16]	6123	66.6	5.5	High: 0.96 g/kg/day; Low: 0.36 g/kg/day	Mean 74.3	Lower total and animal protein intake was associated with increased risk of CKD (highest tertile vs. lowest for total protein OR, 1.16; 95% CI, 1.05–1.30)
Cirillo <i>et al.</i> 2014 [13]	1522	49.3	12	High ≥ 1.6 g/kg/day; Low < 1.0 g/kg/day	Mean 84.0	HP was associated cross-sectionally with higher eGFR, but longitudinally with greater eGFR decline over time
Lew <i>et al.</i> 2016 [14]	60 198	56.5	15.5	Divided into quartiles (fourth group: 65.3 g/day)	N.D	Protein intake amount, especially consumption of red meat was strongly associated with ESRD risk

Nephrol Dial Transplant (2019) 1–4
doi: 10.1093/ndt/gfz216



High-protein diet is bad for kidney health: unleashing the taboo

Kamyar Kalantar-Zadeh¹, Holly M. Kramer² and Denis Fouque³

¹Division of Nephrology, Hypertension and Kidney Transplantation, University of California, Irvine, Orange, CA, USA, ²Department of Preventive Medicine, Loyola University Chicago, Maywood, IL, USA and ³Department of Nephrology, Hosp. Saint-Louis, Lyon, France

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How often have you been told to eat more protein and fewer carbohydrates to stay healthy? This is not an emerging but rather a prevailing dogma in our society. Physicians and other health care professionals tell us about the advantages of a high-protein diet (HPD), such as weight loss, burning calories, diminishing appetite, managing obesity, managing metabolic syndrome and diabetes. This contemporary creed has gone so far that we are continuously pressured to eat more protein and fewer carbohydrates. This is not a new diet. It is a diet that has been around for decades. It is a diet that has been recommended for decades. It is a diet that has been recommended for decades. It is a diet that has been recommended for decades.

Kalantar-Zadeh, Kramer, Fouque, *NDT* Nov 2019

High-Protein Diet Could Be Harmful, Even for Healthy Kidneys

Pam Harrison

November 27, 2019

A high-protein diet, often recommended as a way to lose weight and stay healthy, appears to be harmful to the kidneys in individuals with apparently normal kidney function, two separate new studies indicate.

The two studies, from the Netherlands and Korea, were published online in *Nephrology Dialysis Transplantation*.

Many previous studies have shown that a high-protein diet may harm kidney function, and this is why nephrologists recommend patients with known early stage chronic kidney disease (CKD) stick to a low-protein diet.

But people who have mild CKD of which they are unaware or those at high risk may follow the trend of eating a protein-rich diet because they believe it is healthy, say Kamyar Kalantar-Zadeh, MD, PhD, and colleagues in an accompanying editorial.

"The high-protein culture has emerged as the preferred, healthy, and safe way of eating at the dawn of the 21st century," they write.

Dietary regimens such as the Atkins, Zone, South Beach, and Ketogenic diets have emerged "in which daily protein intake

www.medscape.com

[Nephrol Dial Transplant](#), 2019 Nov 7.

High-protein diet is bad for kidney health: unleashing the taboo.

[Kalantar-Zadeh K¹](#), [Kramer HM²](#), [Fouque D³](#)

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¹Division of Nephrology, Hypertension and Kidney Transplantation, University of California, Irvine, Orange, CA, USA, ²Department of Preventive Medicine, Loyola University Chicago, Maywood, IL, USA and ³Department of Nephrology, Hosp. Saint-Louis, Lyon, France

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EurekAlert (press release)
High-protein diets may harm your kidneys
A high-protein diet is believed to be healthy. ... Kamyar Kalantar-Zadeh, Holly M Kramer and Denis Fouque [1] now consider it necessary to ...
3 weeks ago

Medscape
High-Protein Diet Could Be Harmful, Even for Healthy Kidneys
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High-Protein Diet Could Be Harmful, Even for Healthy Kidneys

Pam Harrison
November 27, 2019

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MDRD: Modification of Diet in Renal Disease

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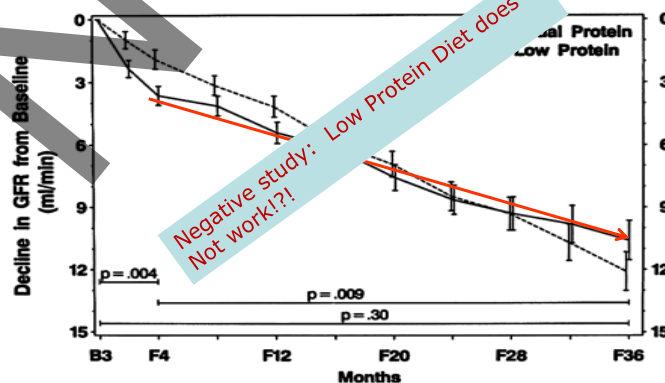
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THE NEW ENGLAND
JOURNAL of MEDICINE

Negative study:
Low Protein Diet
does Not work!?!?

MDRD: Modification of Diet in Renal Disease

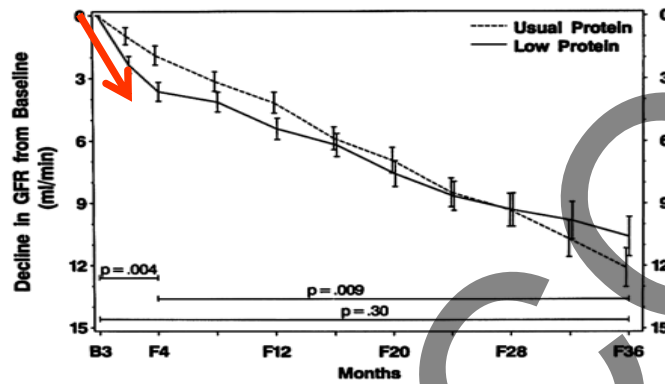
MDRD study 1: secondary analysis



Levey AS et al, J Am Soc Nephrol 1999; 10: 2426-2439

MDRD: Modification of Diet in Renal Disease

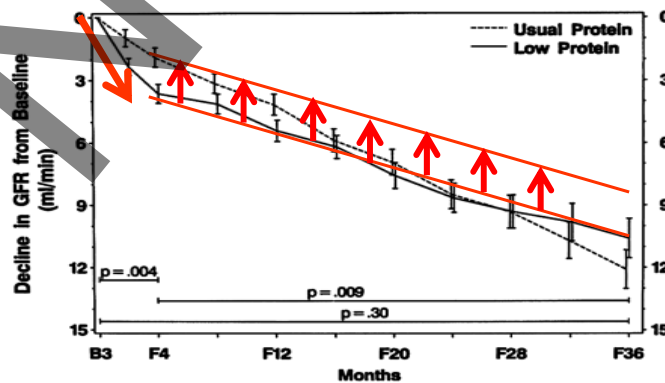
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MDRD: Modification of Diet in Renal Disease

MDRD study 1: secondary analysis



Levey AS et al, J Am Soc Nephrol 1999; 10: 2426-2439

Letter to NEJM re Kalantar-Zadeh & Fouque paper:

Is there an Additive Effect of Low Protein Diet on ACEi/ARB Therapy?

TO THE EDITOR: Kalantar-Zadeh and Fouque address the possible, although still debated, role of restricting dietary protein intake in reducing proteinuria and slowing the progression of chronic kidney disease. Not discussed, however, is whether there is a role for low-protein diets in the modern era of treatment with angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs). Data regarding the additive effect of a low-protein diet and these two drug classes on proteinuria are limited.^{1,2} It is unclear how low-protein diets compare with appropriate use of ACE inhibitor or ARB treatment or whether the combination of a low-protein diet and drugs that block the renin-angiotensin-aldosterone system confers any added benefit in slowing the progression of chronic kidney disease. Low-protein diets may alleviate metabolic disturbances in some patients with chronic kidney disease, but whether such diets

medications that interfere with the renin-angiotensin-aldosterone system is unknown.

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No potential conflict of interest reported.

1. Gansevoort et al. *Am J Kidney Dis* 2000;35:1016-1024.
2. Koppe, L. and D. Fouque (2019). "The Role for Protein Restriction in Addition to Renin-Angiotensin-Aldosterone System Inhibitors in the Management of CKD." *Am J Kidney Dis* 73(2): 248-257.

NEJM.ORG FEBRUARY 8, 2018

The New England Journal of Medicine

THE NEW ENGLAND JOURNAL OF MEDICINE

35

Additive Effect of Low Protein Diet on ACEi/ARB Therapy

Study	Description	ACEi/ARB	Effect
HUMAN Studies			
Ruilope et al, 1982	N=17 pts proteinuria >3 g/d, 3 weeks LPD <1.0 g/kg/d +/- Enalapril (20 mg daily)	Enalapril (10 mg/d)	Addition of enalapril led to further ↓ proteinuria and ↓ filtration fraction, whereas K, PRA, GFR, and RPF values increased
Gansevoort et al, 1995	Open label randomized controlled trial (n=14 pts proteinuria > 3g/d): LPD vs ACEi vs. LPD+ACEi	Enalapril (10 mg/d)	↓ proteinuria
Chin et al, 2015	Open label case-control x 26 weeks, n=174 pts eGFR >30 ml/min	Olmesartan (40 mg/d)	The probability of ↓ albuminuria with ARB was lower in pts with an increased eUUN vs ARB alone
ANIMAL Studies			
Cartwright et al, 1988	¾ subtotal nephrectomized rats, LPD vs. NPD +/- ACEi	Captopril (50 mg/kg/day)	↓ proteinuria and ↓ glomerular lesions
Peters et al, 2000	Mesangioproliferative GN model in rats: LPD vs NPD +/- ACEi/ARB	Enalapril (100 mg/l) or losartan (100 mg/l) drinking water	↓ TGF-β overexpression in glomeruli, ↓ proteinuria, ↓ glom. matrix accumulation & over-production of fibronectin & PAI-1
Zhang et al, 2016	¾ subtotal nephrectomized rates, LPD vs. NPD		Mesangial cells treated with serum of LPD rats, ↓ expression of Ang II, AT1R, fibronectin, TGF-β

Kalantar-Zadeh K and Fouque D. Nutritional Management of Chronic Kidney Disease. *N Engl J Med.* 2018;378(6):584-585.

American Journal of Clinical Nutrition 2013
**Reconciling Low Protein Intake with Nutritional Therapy:
 Is there Risk of Malnutrition?**

AJCN. First published ahead of print May 1, 2013 as doi: 10.3945/ajcn.112.036418.

American Journal of Clinical Nutrition 2013 **AJCN 2013**
 Narrative Review

Kovesdy, Kopple and Kalantar-Zadeh
**Management of PEW in NDD-CKD: Reconciling
 LP Intake with Nutritional Therapy**

Management of protein-energy wasting in non-dialysis-dependent
 chronic kidney disease: reconciling low protein intake with
 nutritional therapy¹⁻⁴

Csaba P Kovesdy, Joel D Kopple, and Kamyar Kalantar-Zadeh

Protein Requirements in Health vs. CKD

- Normal adult requirement:
 - ... → **0.46 g/kg/d** if Essential AA provided → 0.6 g/kg/day
 - **RDA (recommended dietary allowance): 0.8 g/kg/day**
 - Estimated from average protein need of non-pregnant, non-lactating healthy adults: ~0.6 g/kg/day
 - Protein of unselected or mixed biological value
 - Plus **33% to obtain safe intake**, hence: $0.6 + 0.2 = 0.8$
 - FAO/WHO & Food and Board of the National Academy of Sciences recommendation
- Nonnephrotic adult CKD patients
 - With no superimposed catabolic illnesses
 - **Hence: Similar requirement as normal healthy adult!**

based on Kovesdy, Kopple & Kalantar-Zadeh. *Am J Clin Nutr.* 2013;97(6):1163-77

Low Protein Diet (LPD): 0.6-0.8 g/kg/day VERY Low Protein Diet (VLPD): 0.3-0.4 g/kg/day + supplement

- For stable (e.g., nonnephrotic, noninflamed/noncatabolic) NDD-CKD patients:
 - **0.6 – 0.8 g protein/kg/day**
 - **≥ 50% of protein is of High Biological Value (HBV)**
 - HBV are often considered **animal** origin:
 - Poultry, meat, eggs, fish, cheese, milk
 - Low biological value proteins (?): Legumes, grains, nuts, seeds, vegetables
 - *However: some studies suggest superiority of plant diet in CKD!*
 - **We still suggest >50% of protein source be plant-based.**
 - *If strict vegan diet (as opposed to lacto- ovo- vegetarian) or if VLPD is given, then supplements may be needed (?)*

based on Kovesdy, Kopple & Kalantar-Zadeh. *Am J Clin Nutr.* 2013;97(6):1163-77

What is High Biologic Value (HBV) Protein?

Kalantar-Zadeh *et al.* 25 Dietary Restrictions
Tables Biologic Value of selected food items

Table 1. Biologic value of selected protein-rich foods. On a scale of 1 to 100, representing the highest efficiency. Foods with high biologic value (HBV) have a biologic value >75 (Source: Wikidoc on line: www.wikidoc.org/index.php)

	Ile	Leu	Val	Met	Cys	Biologic Value
Whole egg	1.0	1.0	1.0	1.0	1.0	100*
Milk, human	0.9	0.9	0.9	0.9	0.9	97*
Wheat, beef	0.8	0.8	0.8	0.8	0.8	67*
Soybeans	0.7	0.7	0.7	0.7	0.7	67*
Rice	0.6	0.6	0.6	0.6	0.6	60*
Wheat	0.5*	0.4*	1	1	1	60*

Can plant-based diet provide the needed High Biologic Value Proteins?
 Vegan proteins have low biological value and high potassium
 Animal protein have high phosphorus and high acidogenicity
 Hence, **CKD specific Supplement (keto-analogues)** are needed with **(v)LPD (0.6-0.8 g/kg/day, or lower)**

Kalantar-Zadeh... Kovesdy, *BMC Nephrol* 2016

Energy & Nutrient Recommendations in NDD-CKD: What about Calorie?

- Patients aged < 60 y.o.
 - ~35 kcal/kg/day
- Patients aged ≥ 60 y.o.
 - 30 (-35) kcal/kg/day (??)
- Low potassium <3 g/day (4.7 g/day if no hyper-K)
- Low phosphorus <800 mg/day
- Low sodium <2.3 g/day (less stringent: <3-4 g/day)

From Presentation by Amanda Brown, RD 6/2014
based on Kovesdy, Kopple & Kalantar-Zadeh. *Am J Clin Nutr.* 2013;97(6):1163-77
Kalantar-Zadeh & Foque, *Nutritional Management of CKD. NEJM* Nov 2, 2017

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Kalantar-Zadeh & Foque, *Nutritional Management of CKD. NEJM* Nov 2, 2017

Barriers in the Managements to Low Protein Diet Therapy for the of CKD in the Elderly

Challenge 4:

Some nephrologists do not know how to monitor protein-restricted dieting!

“24-hr urine collection is rarely ordered by contemporary nephrologists, who tend to order only “spot” urine protein to creatinine ratio!”

Periodic 24-hr urine

→ To Monitor Food Intake Adherence

Check **24 hr urine VOLUME** (1 Lit = 10 dL = 1000 ml)

- **Urine Urea Nitrogen (UNN)** → x 6.25 ...
- **Sodium** (<4 g/day or <2.3 g/day) → mmol/44 ...
- **Potassium** (<3/day only if high risk of hyper-K) → mmo/25 ...
- **Creatinine** (1-2 grams/day)
- **Protein**
- **Albumin** (in addition to protein)
- Others, e.g. kidney stone studies (citrate, oxalate, uric acid, Ca, phos, Mg, cysteine) but usually not necessary
- Calculate creatinine index to ensure there is no under or overcollection:
 - 24 hr creatinine excretion **Men**: 1.5-2.5 g/day (or 20-30 mg/kg BW)
 - 24 hr creatinine excretion **Women**: 1.-1.5 g/day (or 10-20 mg/kg BW)

From Presentation by Amanda Brown, RD 6/2014
based on Kovesdy, Kopple & Kalantar-Zadeh. Am J Clin Nutr. 2013;97(6):1163-77

Barriers in the Managements to Low Protein Diet Therapy for the of CKD in the Elderly

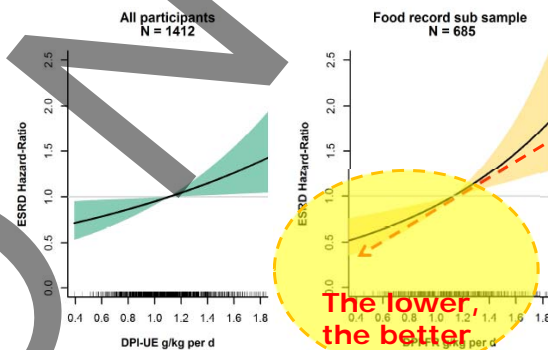
Challenge 5:

Keto-analogues and hydroxy-analogues of amino-acids are often misunderstood and underutilized.

Understand the biology and physiology of keto- and hydroxy-analogues of amino acids

How low can Dietary Protein Intake (DPI) go?

DPI: 1.0 to 0.8 ... → ... 0.8 to 0.6... → ... <0.6 g/kg/day?



Metzger M, Yuan WL, Haymann J-P, Flamant M, Houillier P, Thervet E, Boffa J-J, Vrtovsnik F, Froissart M, Bankir L, Fouque D and Stengel B. Association of a low-protein diet with slower progression of chronic kidney disease. *Kidney International Reports*. 2017. doi: 10.1016/j.ekir.2017.08.010. PubMed PMID. URL: <http://dx.doi.org/10.1016/j.ekir.2017.08.010>.

Most importantly, the absence of threshold for the relation between DPI and ESRD risk indicates there is no optimal DPI in the range observed in this cohort [so that even if one eats less protein than usual, e.g. going from 1.2-1.4 grams/kg/day (current average US Americans' protein intake) to 0.8-1.0 grams/kg/day, risk of ESRD is lowered]

KK2

Supplemented Very Low Protein Diet (sVLPD)

- What would be equivalent of ~0.6 g protein/kg/day?
 - 0.3 g/kg/day comes from protein of animal products
 - Additional 0.28 g/kg/day is from ketoacids and hydroxyacid analogues
 - 9 essential amino acids (EAAs) → ketoacid analogues of EAAs
 - 4 EAAs + 4 ketoacid and 1 hydroxy-acid analogues of EAAs
- Supplementing with ketoacids and hydroxyacid analogues of EAAs is indicated for patients unable to adhere to low-protein diets

based on Kovesdy, Kopple & Kalantar-Zadeh. *Am J Clin Nutr.* 2013;97(6):1163-77

AJKD

Perspective

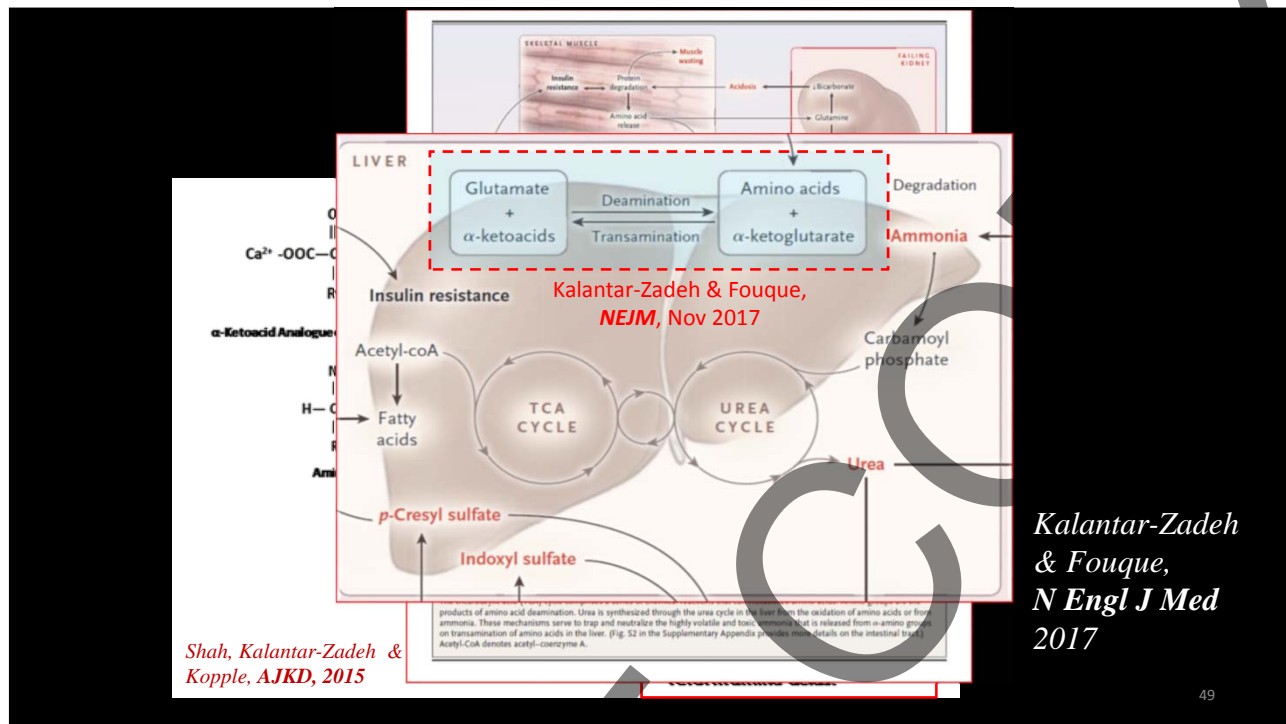
AJKD 2015

Is There a Role for Ketoacid Supplements in the Management of CKD?

Anuja P. Shah, MD,¹ Kamyar Kalantar-Zadeh, MD, PhD,² and Joel D. Kopple, MD^{1,3}

Ketoacid (KA) analogues of essential amino acids (EAAs) provide several potential advantages for people with advanced chronic kidney disease (CKD). Because KAs lack the amino group bound to the α carbon of an amino acid, they can be converted to their respective amino acids without providing additional nitrogen. It has been well established that a diet with 0.3 to 0.4 g of protein per kilogram per day that is supplemented with KAs and EAAs reduces the generation of potentially toxic metabolic products, as well as the burden of potassium, phosphorus, and possibly sodium, while still providing calcium. These KA/EAA-supplemented very-low-protein diets (VLPDs) can maintain good nutrition, but the appropriate dose of the KA/EAA supplement has not been established. Thus, a KA/EAA dose-response study for good nutrition clearly is needed. Similarly, the composition of the KA/EAA supplement needs to be reexamined; for example, some KA/EAA preparations contain neither the EAA phenylalanine nor its analogue. Indications concerning when to inaugurate a KA/EAA-supplemented VLPD therapy also are unclear. Evidence strongly suggests that these diets can delay the need for maintenance dialysis therapy, but whether they slow the loss of glomerular filtration rate in patients with CKD is less clear, particularly in this era of more vigorous blood pressure control and use of angiotensin/aldosterone blockade. Some clinicians prescribe KA/EAA supplements for patients with CKD or treated with maintenance dialysis, but with diets that have much higher protein levels than the VLPDs in which these supplements have been studied. More research is needed to examine the effectiveness of KA/EAA supplements with higher protein intakes.

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Barriers in the Managements to Low Protein Diet Therapy for the of CKD in the Elderly

Challenge 6:

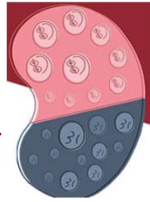
Transition to dialysis should occur gradually “incrementally” with use of low protein diet

Low protein diet and ketoacids to preserve RESIDUAL KIDNEY FUNCTION (RKF) longer!

Residual Kidney Function (RKF) upon Transition and Dialysis Patients

Therapeutic options

- Avoidance of nephrotoxins
- RAAS blockade
- BP control?
- Avoidance of hypovolemia
- ↓ Peritonitis in PD
- Twice-Weekly HD?
- Low protein diet ?



Benefits of RKF

- ↑ middle molecule & uremic toxins
- Maintenance of liquid balance
- Improved BP control & ↓ in LVH
- Endocrine: Epo, Ca⁺⁺, Pi, VitD3
- ↓ Malnutrition and inflammation
- ↓ Survival & quality of life

Am J Kidney Dis 53:1068-1081. © 2009

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Nutritional Management of Incremental HD: strategies for dialysis commencing: **once weekly** → **2x/week** → **3x/week**

	Once-a-week	Twice-a-week	Thrice-a-week
Nutritional support	+++	++	+
Protein intake	Reduced (6 out of 7 days): sVLPD	Reduced (5 days): sVLPD or LPD	increased
Energy intake	increased	increased	increased
vascular access compromise	+	++	+++
Protection of residual renal function	+++	++	-/+
"Counter-Physiologic" effect of HD treatment	+	++	+++
HD scheduling challenge	+	++	-
Costs and reimbursement	+	++	+++

Modified from: Caria S, Cupisti A, Sau, *Bolascio BMC Nephrol* 2014;15:172
Bolascio, Cupisti, Locarelli, Caria, Kalantar-Zadeh, *J Ren Nutr.* 2016 26:352-359

Barriers in the Use of Plant-Based Diet in DKD

Challenge 7:

It is often believed that plant-based foods, fruits and vegetables have low biologic value proteins and high potassium

Diversify and better combine plant-based diet -
Use potassium binder instead of "low potassium diet"

CKD Patients: ↑ Plant-Protein Ratio → ↓ Mortality?

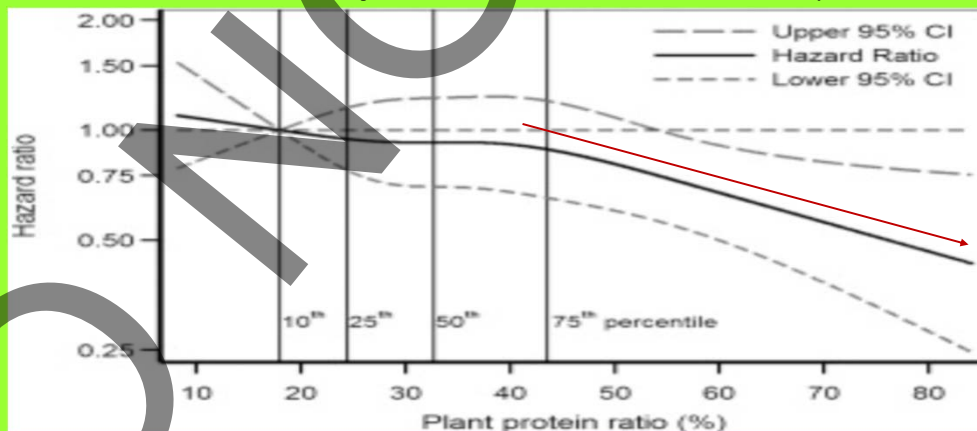


Figure 3. Restricted cubic spline of mortality association of plant protein ratio in the estimated glomerular filtration rate < 60 mL/min/1.73 m₂ subpopulation.

Xiaorui Chen, Guo Wei, Thunder Jalili, Julie Metos, Ajay Giri, Monique E. Cho, Robert Boucher, Tom Greene, Srinivasan Beddhu. The Associations of Plant Protein Intake With All-Cause Mortality in CKD, *American Journal of Kidney Diseases*, 2015, <http://dx.doi.org/10.1053/j.ajkd.2015.10.018>

>2/3 of Pro

- A diet in which proteins from
 - urea generat
 - inflammatio
 - acidosis is be
 - very little ab
 - Better bowe

Thus a vegeta protein dietary

Can plant-based diet provide the needed High Biologic Value Proteins?

Vegan proteins have adequate biological value and high potassium should not pose an issue given high fibers to enhance bowel movement + use potassium binders

Fight the wrong dogma of "avoid fruits/vegetables in CKD"

Consider adding Keto-/Hydroxy-analogues of AA

Planning to celebrate Diwali?

Challenging the wrong dogma of "avoid high-potassium fruits/vegetables" on #Diwali. Eat healthy, eat high fiber, eat more fruits & vegetables, and control potassium without imposing dietary restrictions of healthy food

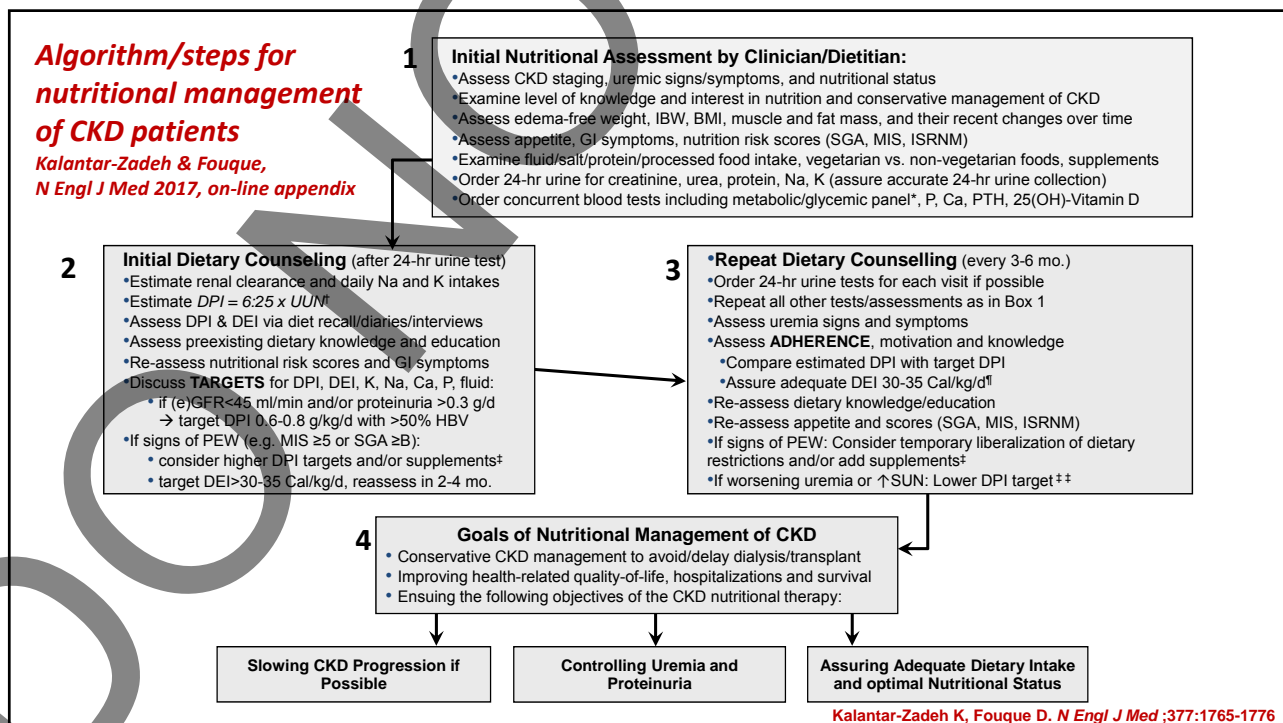
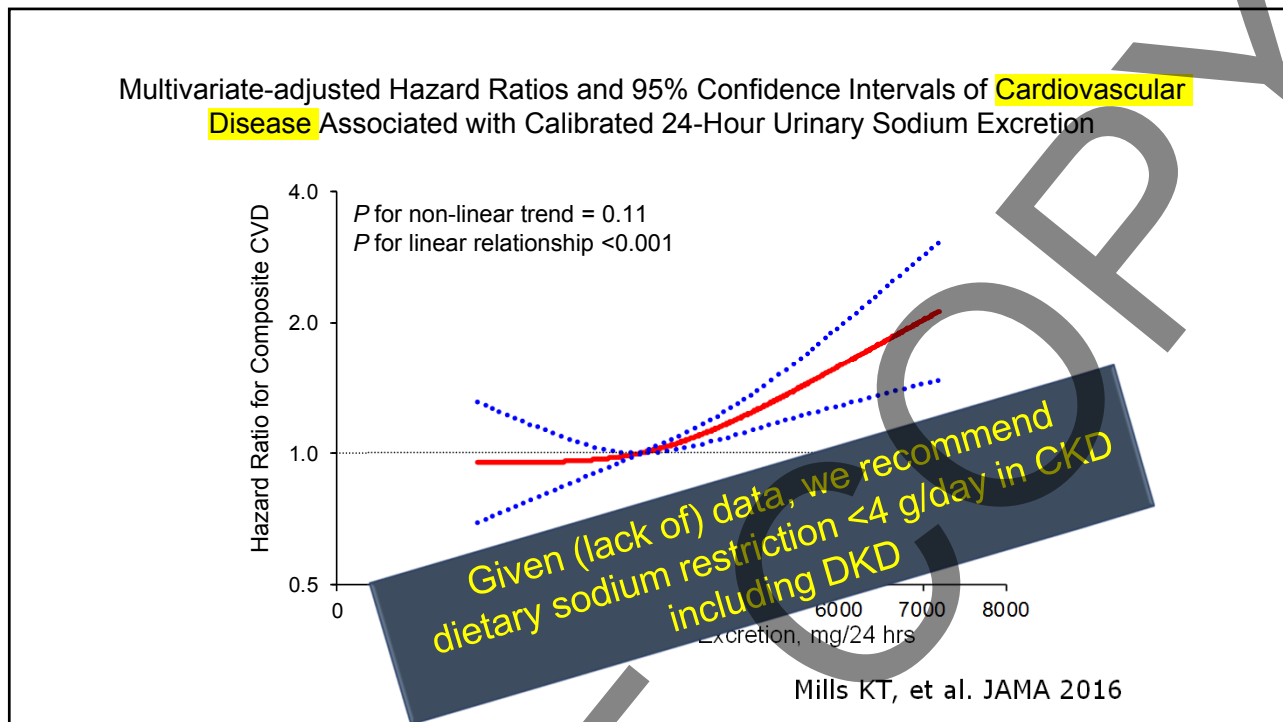
Planning to celebrate Diwali?

... what you should know... health scare around the quality of market, more people are turning towards dry fruit

anted that for all

Part 7

Sodium Intake in CKD/DKD



Conclusions: Lifestyle and Diet in CKD

- Lifestyle modification can be recommended to persons with DKD and any other CKD
- Alternative nutritional approaches to CKD/DKD management should be used and innovated such as **nutritional management of CKD** to add to the armamentarium of the CONSERVATIVE & PRESERVATIVE MANAGEMENT of CKD.
- Low Protein Diet (LPD) of **0.6-0.8 g/kg(IBW)/day** should be the target for **non-dialysis-CKD/DKD** patients Stages **3b-5** and all **proteinuric** patients including DKD (**A3** albuminuria >0.3 g/d) with high-biologic value protein and adequate **energy** and **micronutrients** and **>50% from plant-based sources**.
- At least 50% of the CKD diet should be from **plant-based** diet, and the wrong dogma of restricting fruits and vegetables for the fear of **hyperkalemia** should be opposed
- Dietary sodium in CKD/DKD can be **<3-4 g/day**. Targeting <2.3 g/day can be too stringent.

Summary of recent developments: Revisiting the old concept of renal nutrition within the Contemporary Framework

1. US Government Executive Order of July 10, 2019
2. World Kidney Day 2020: Focus on Secondary and Tertiary Prevention
3. KDOQI Guidelines 2020: CKD
4. Recent data suggesting harm caused by high protein diet, focus on kidney health
5. More Conservative/Preservative Approaches (avoid the term "predialysis")
6. More attention diabetes and DKD: LPD and keto-analogues vis-à-vis insulin sensitivity and obesity
7. Patient-centric, Individualized approach across different patients characteristics (age, gender, race)
8. Nephrologist and dietitian synergy
9. Protein-Energy Wasting and Sarcopenia
10. Revisiting Old Lit.: MDRD

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SAVE THE DATE **UCI Health**

Nutritional and Dietary Management of Kidney Disease: A Patient Care Approach

We Are What We Eat: Learn How to Enforce Kidney Health through Nutrition and Diet

Saturday, February 29, 2020
7:30 a.m. to 4:45 p.m.

UCI Nephrology has teamed up with the nation's leading experts to leverage their interests and expertise to provide insights on real-world clinical management and hands-on workshops for dietary approaches.

UCI Health Medical Center
Bldg. 53, Auditorium
101 The City Drive South
Orange, CA 92868

For more information,
Kristine Fuentebella at kfuenteb@uci.edu | 714-456-5142

This is a full-day CME course for physicians (Nephrologists, Internists, Urologists and Family Practitioners) and other healthcare providers and allied health professionals (dietitians, nurses, nutritionists, and researchers) who will learn the pathophysiology and mechanisms related to the role of nutrition in kidney disease and kidney health.

Nutritional and Dietary Management of Kidney Disease: A Patient Care Approach

- **We are what we eat: Learn how to enforce kidney health through nutrition and diet**
- **Saturday, Feb. 29, 2020 – 7:30 am - 4:45 pm**
- **University of California Irvine (UCI) Medical Center, Bldg. 53, Auditorium 101**
- **The City Drive South, Orange, California 92868, USA**
- **UCI Nephrology has teamed up with the nation's leading experts to leverage their interests and expertise to provide insights on real-world clinical management and hands-on workshops for dietary approaches.**
- **This is a full-day CME course for physicians (nephrologists, internists, urologists and family practitioners) and other healthcare providers and allied health professionals (dietitians, nurses, nutritionists and researchers) who will learn the pathophysiology and mechanisms related to the role of nutrition in kidney disease and kidney health.**

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