Plant-Based Diets in Kidney Disease

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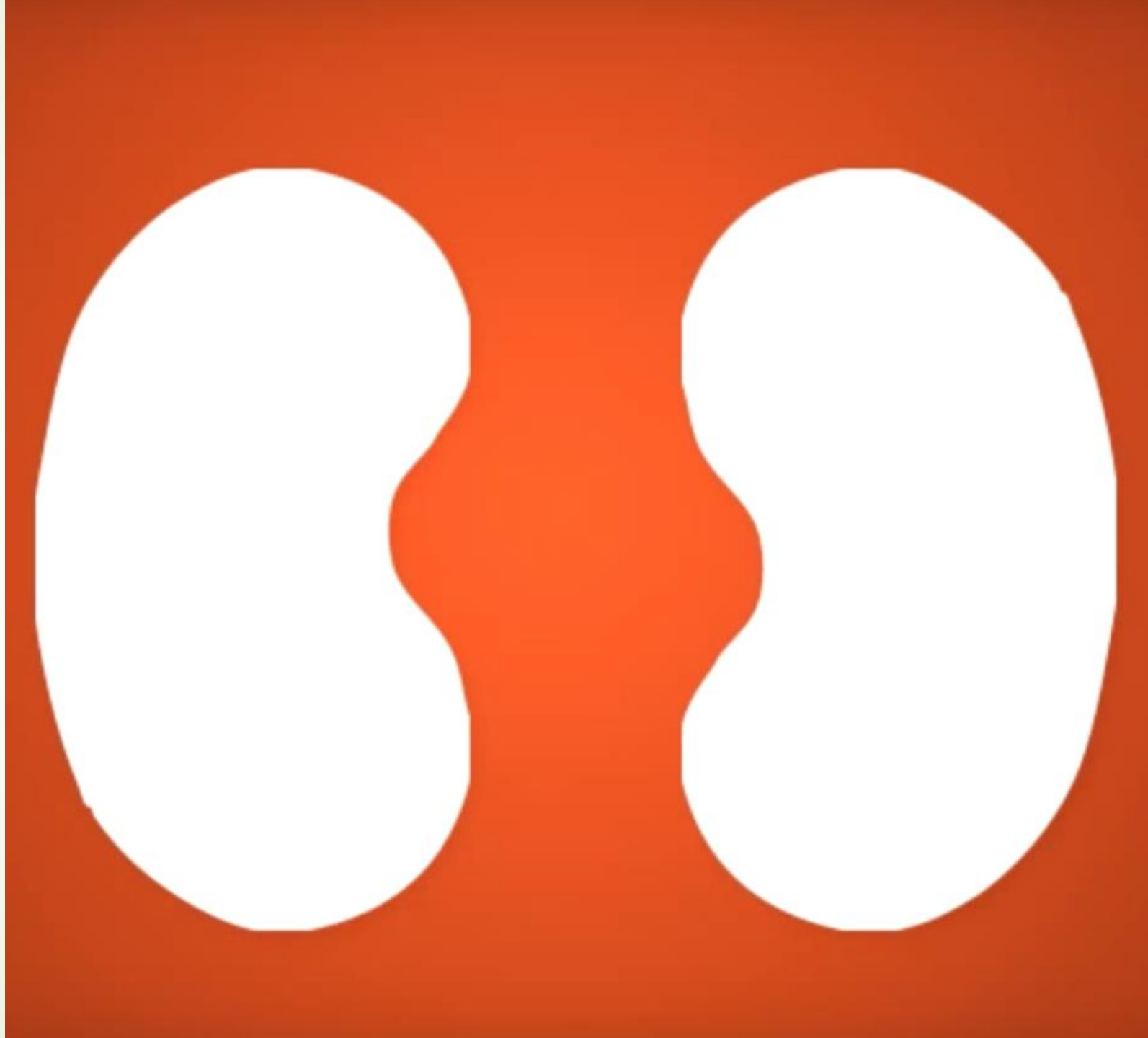
Financial Disclosures

- Consulting:
  - Insyght Interactive
  - Vifor Pharma
  - Otsuka
- I eat a plant-based diet (quite happily too)



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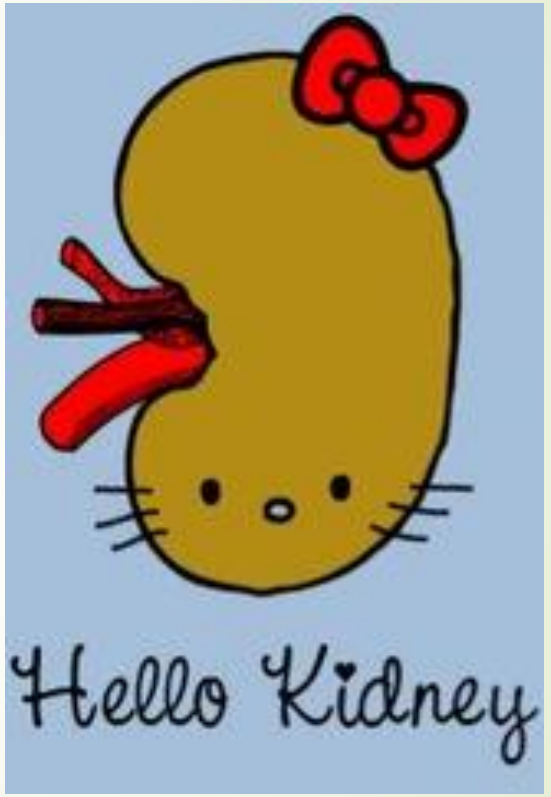
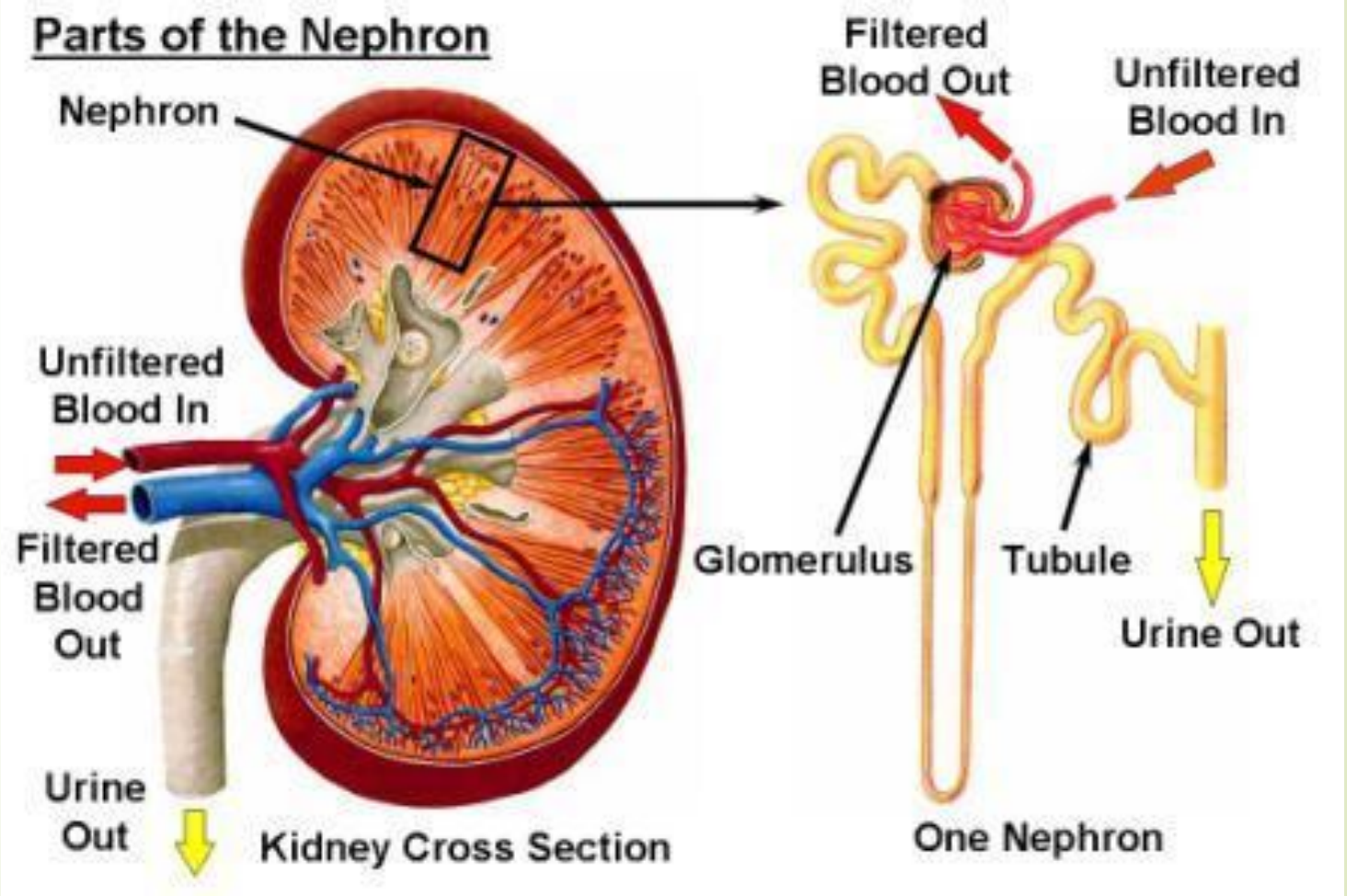
Kidney Basics



Inside the Kidney

- Filtering Unit (nephron)
- Composed of glomerulus (filter) and tubules (absorb/secrete substances)
- Each kidney has a million nephrons



How is kidney disease diagnosed?

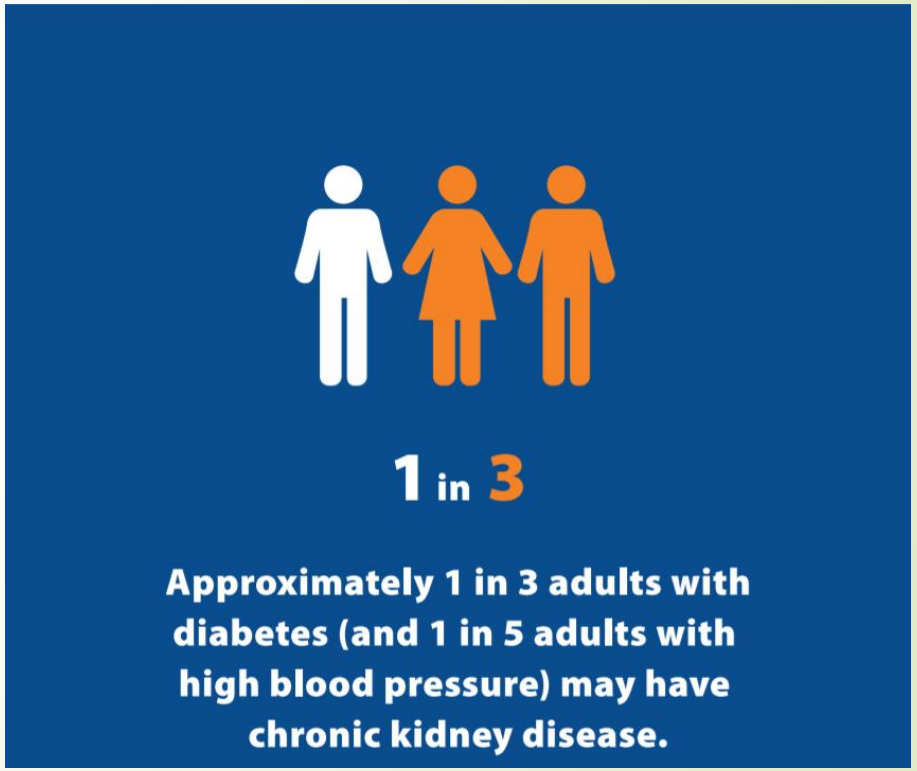
1. A blood test is done to measure your **creatinine** level
2. The creatinine level is then used in a mathematical equation to calculate your **eGFR**
3. eGFR determines your **level** of kidney function (or dysfunction)

Stages of Kidney Disease

- Stage 1: GFR > 90
- Stage 2: GFR 60 - 90
- Stage 3: GFR 30 - 60
- Stage 4: GFR 15 - 30
- Stage 5: GFR 0 – 15
  - End Stage Renal Disease: Stage 5 but on dialysis

GFR roughly correlates to % kidney function

Chronic Kidney Disease Prevalence



Murphy D, McCulloch CE, Lin F, et al. Trends in prevalence of chronic kidney disease in the United States. *Annals of Internal Medicine*. 2016;165(7):473–481.
https://www.cdc.gov/kidneydisease/pdf/kidney_factsheet.pdf

Plant-Based Diet Basics

What is a plant-based diet?

- No exact definition
- Doesn't mean you have to be vegan or even vegetarian
- Your diet is just mostly plants
- Another way to say it is that you are eating less meat/dairy than the standard American diet

What is a plant-based diet?

- Terms with the same meaning as plant-based:
  - Plant-Dominant
  - Plant-Strong
  - Plant-Supportive
  - Plant-Leaning
  - Plant-Forward
  - Plant-Powered
- They all mean that plants are the focus of the plate

What is a plant-based diet?

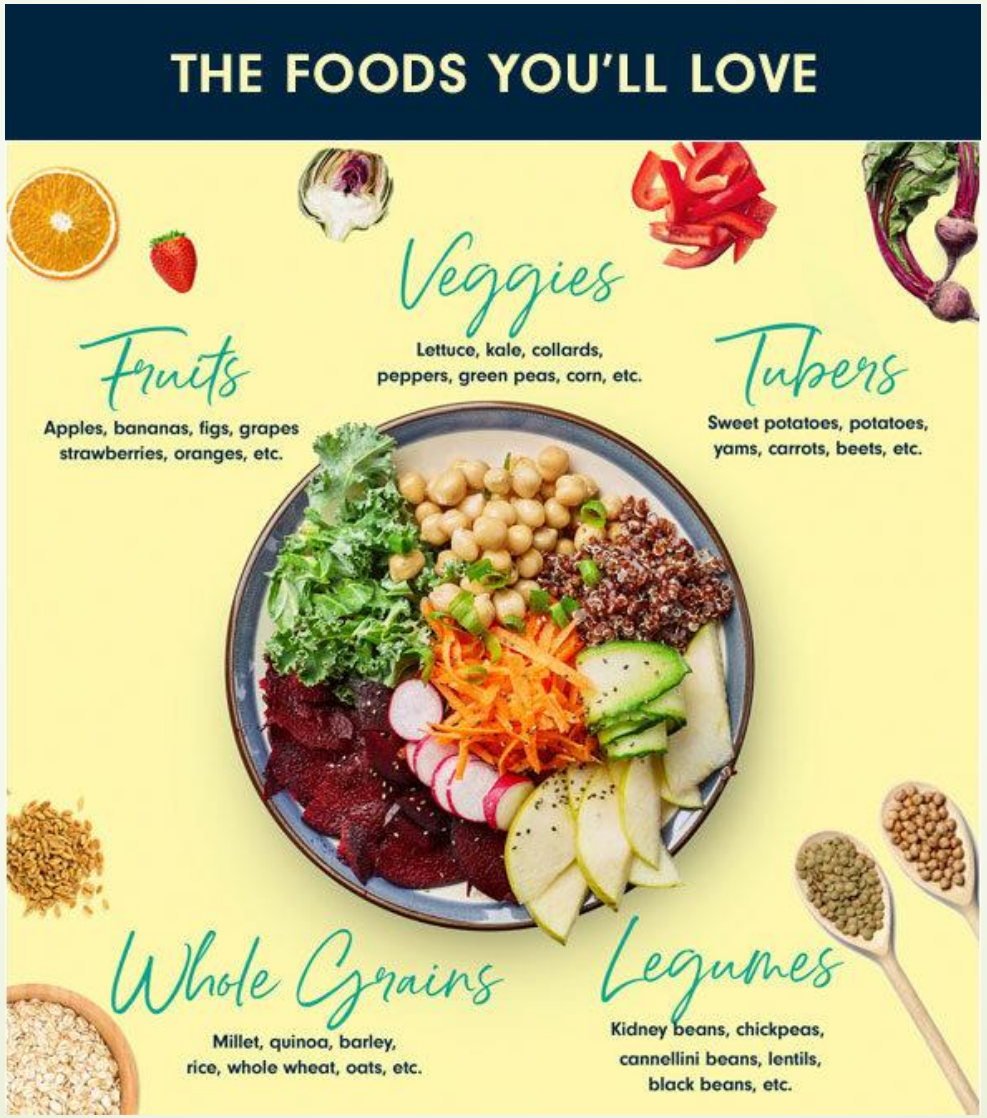
- Examples of a plant-based diet:
  - Mediterranean
  - Vegetarian
    - Lacto-vegetarian
    - Ovo-vegetarian
    - Lacto-ovo-vegetarian
  - Flexitarian
  - Pescatarian
  - Reducetarian
  - Vegan
  - DASH
  - Whole-food, plant-based

Plant-Based Can Still Be Unhealthy

Unhealthy

Healthy

What can you eat on a plant-based diet?



Forks Over Knives

Potential Benefits of a Plant-Based Diet in Kidney Disease

Prevention of the Causes of Kidney Disease:
Type 2 Diabetes
Hypertension
Obesity

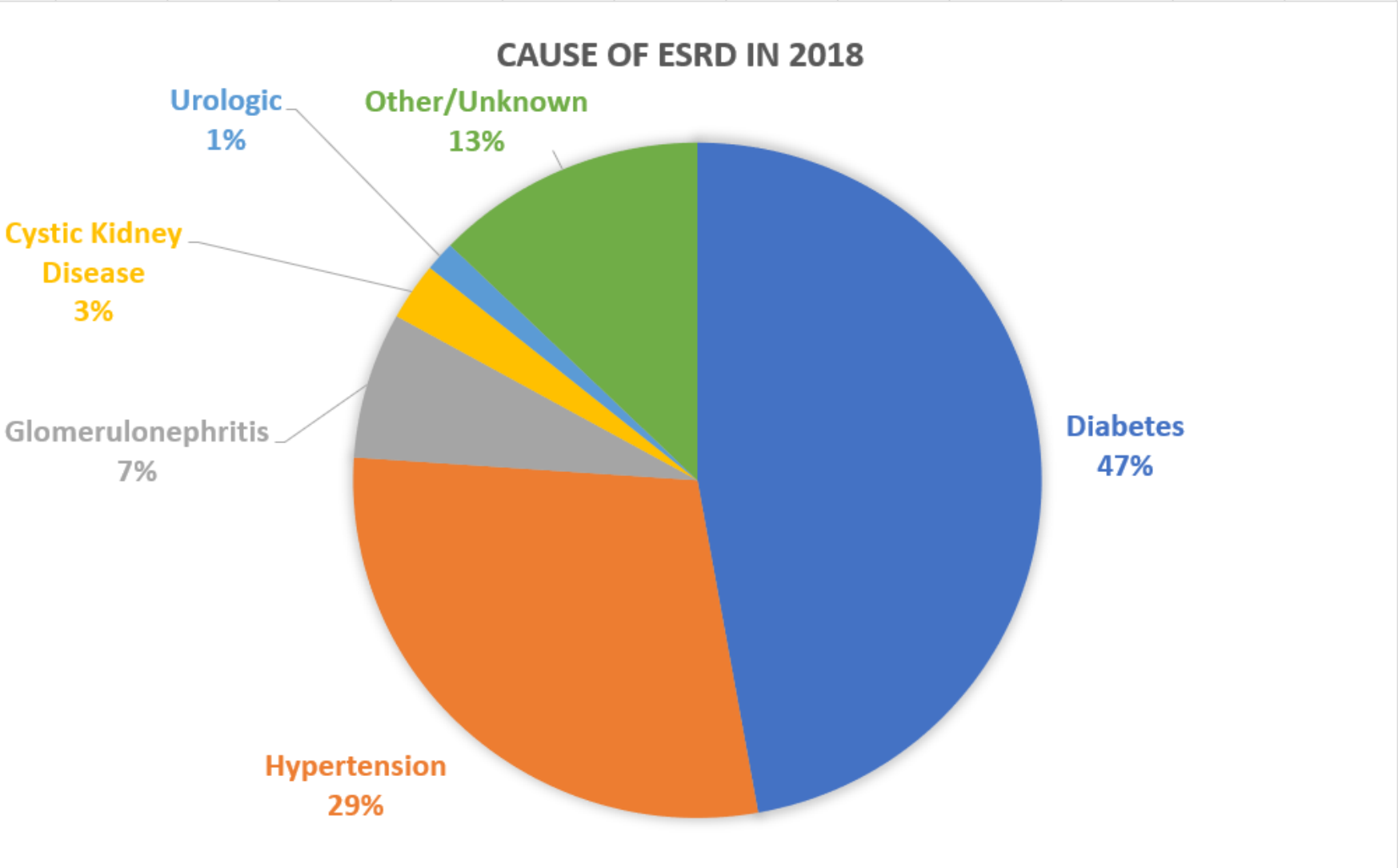
Attenuation of Kidney Disease Progression:
eGFR decline
Albuminuria

Reduction of Kidney Disease Complications:
Hyperphosphatemia
Metabolic Acidosis
Renal Hypertension
Uremic Toxins
Cardiovascular Longevity

Joshi S, McMacken M, Kalantar-Zadeh K. "Plant-Based Diets for Kidney Disease: A Guide for Clinicians." *American Journal of Kidney Diseases* 77.2 (2021): 287-296.

Causes of Kidney Disease

Causes of ESRD (End-Stage Renal Disease)



USRDS

Why Do Plant-Based Diets Help with Preventing and Treating Diabetes and Obesity?

Obesity

- Increased fiber
- Lower caloric density
- Lower daily caloric intake
- Reduced fat intake
- Reduced processed food intake
- Reduced sugar intake

Type 2 Diabetes Mellitus

- Weight loss
- Improved insulin sensitivity
- Lower glycemic index
- Increased insulin secretion

Turner-McGrievy, Gabrielle, Trisha Mandes, and Anthony Crimarco. "A plant-based diet for overweight and obesity prevention and treatment." *Journal of Geriatric Cardiology: JGC* 14.5 (2017): 369.

McMacken, Michelle, and Sapana Shah. "A plant-based diet for the prevention and treatment of type 2 diabetes." *Journal of Geriatric Cardiology: JGC* 14.5 (2017): 342.

Hypertension is a *cause* and *complication* of chronic kidney disease

- *Cause:* Hypertension is the second most common cause of kidney disease and kidney failure

- *Complication:* As kidney function declines, sodium excretion becomes impaired causing salt and water retention leading to hypertension (activation of the sympathetic nervous system also plays a role).

Hypertension in America

- 102 million Americans have hypertension
- Prevalence rises with age
  - At age 45 without HTN, 40 year risk is 84-93% of developing HTN, depending on ethnicity[1]

Table 7. Prevalence of Hypertension Based on 2 SBP/DBP Thre

	SBP/DBP ≥130/80 mm Hg or Self-Reported Antihypertensive Medication†	
Overall, crude	46%	
	Men (n=4717)	Women (n=4906)
Overall, age-sex adjusted	48%	43%
Age group, y		
20–44	30%	19%
45–54	50%	44%
55–64	70%	63%
65–74	77%	75%
75+	79%	85%
Race-ethnicity§		
Non-Hispanic white	47%	41%
Non-Hispanic black	59%	56%
Non-Hispanic Asian	45%	36%
Hispanic	44%	42%

[1]Carson AP. Hypertension. 2011;57:1101-7
Table: Whelton, Paul K. *Journal of the American College of Cardiology* (2017): 24430.

Is Hypertension Destiny?

Rural Kenya

Age group.	Blood pressure.		Normal in Europeans and Americans.	
	Aver. syst.	Aver. diast.	Syst.	Diast.
15–19	123·07	81·89	123	80
20–24	122·76	79·99	125	81
25–29	126·37	83·96	126	82
30–34	126·05	84·73	127	83
35–39	125·55	85·86	128	84
40–44	118·32	81·29	129	85
45–49	113·19	75·50	131	86
50–54	109·79	74·09	133	87
55–59	106·59	69·63	135	88
60 and over	105·76	66·98	140+	90+

Rural China

TABLE IV

Group.	Number.	Age.	Systolic pressure.	Diastolic pressure.
			Mean.	Mean.
Chwan Miao ..	143	16–70	109·7	72·1
Ta Hwa Miao .	150	16–70	104·0	70·0
Noso (Lolo) ..	105	16–64	104·5	72·8

Donnison, C. P. "BLOOD PRESSURE IN THE AFRICAN NATIVE.: ITS BEARING UPON THE ÆTIOLOGY OF HYPERPIESIA AND ARTERIO-SCLEROSIS." *The Lancet* 213.5497 (1929): 6-7.
Morse, W. R., and Y. T. Beh. "Blood pressure amongst aboriginal ethnic groups of Szechwan Province, West China." *The Lancet* 229.5929 (1937): 966-968.
www.nutritionfacts.org

Rationale Behind the DASH Diet

DASH TRIAL

Descriptive characteristics of the dietary patterns used in the Dietary Approaches to Stop Hypertension trial

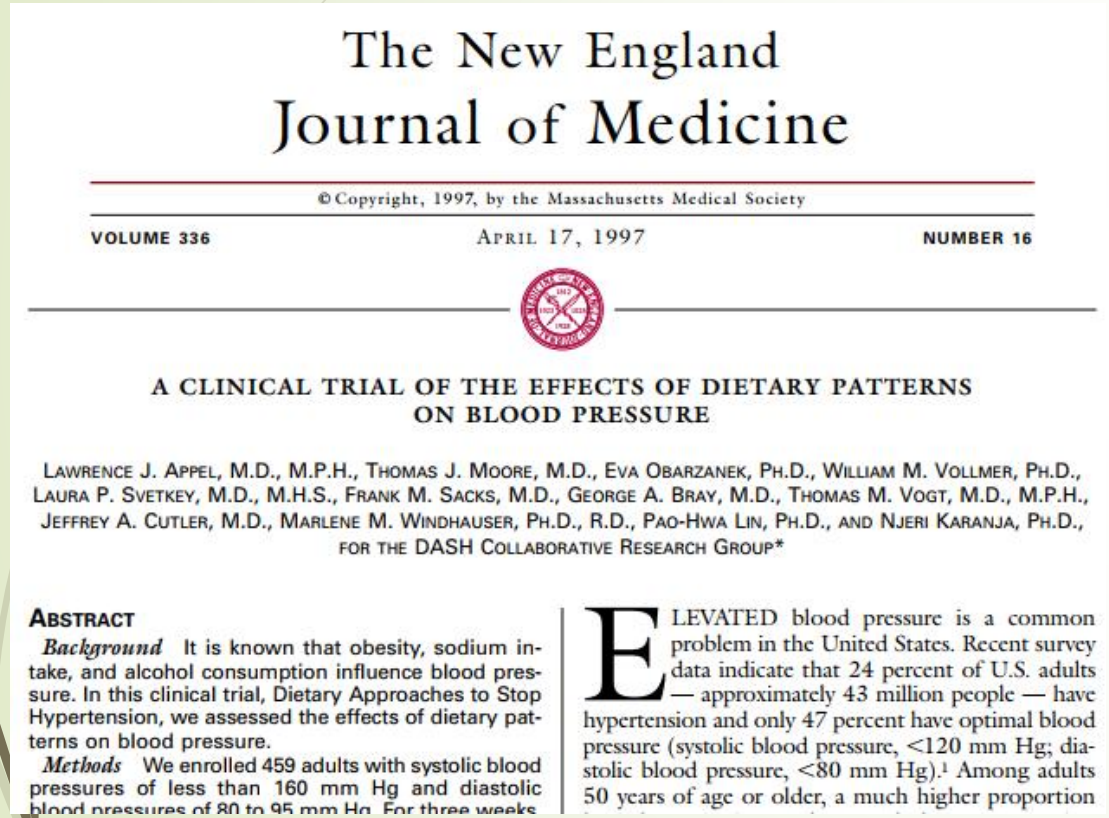
NJERI M. KARANJA, PhD, RD; EVA OBARZANEK, PhD, MPH, RD; PAO-HWA LIN, PhD; MARJORIE L. McCULLOUGH, MS, RD; KATHERINE M. PHILLIPS, PhD; JANIS F. SWAIN, MS, RD; CATHERINE M. CHAMPAGNE, PhD, RD, FADA; KIMBERLY P. HOBEN, MPH, RD; for the DASH Collaborative Research Group

ABSTRACT

Epidemiologic studies demonstrate that certain eating patterns are associated with a lower risk of a variety of

The diet design goals were to create patterns that would (a) have the blood pressure–lowering benefits of a vegetarian diet, yet contain enough animal products to make them palatable to nonvegetarians

DASH Diet



The New England
Journal of Medicine

VOLUME 336 APRIL 17, 1997 NUMBER 16

A CLINICAL TRIAL OF THE EFFECTS OF DIETARY PATTERNS ON BLOOD PRESSURE

LAWRENCE J. APPEL, M.D., M.P.H., THOMAS J. MOORE, M.D., EVA OBARZANEK, PH.D., WILLIAM M. VOLLMER, PH.D., LAURA P. SVETKEY, M.D., M.H.S., FRANK M. SACKS, M.D., GEORGE A. BRAY, M.D., THOMAS M. VOGT, M.D., M.P.H., JEFFREY A. CUTLER, M.D., MARLENE M. WINDHAUSER, PH.D., R.D., PAO-HWA LIN, PH.D., AND NJERI KARANJA, PH.D., FOR THE DASH COLLABORATIVE RESEARCH GROUP*

ABSTRACT

Background It is known that obesity, sodium intake, and alcohol consumption influence blood pressure. In this clinical trial, Dietary Approaches to Stop Hypertension, we assessed the effects of dietary patterns on blood pressure.

Methods We enrolled 459 adults with systolic blood pressures of less than 160 mm Hg and diastolic blood pressures of 80 to 95 mm Hg. For three weeks

ELEVATED blood pressure is a common problem in the United States. Recent survey data indicate that 24 percent of U.S. adults — approximately 43 million people — have hypertension and only 47 percent have optimal blood pressure (systolic blood pressure, <120 mm Hg; diastolic blood pressure, <80 mm Hg).[1] Among adults 50 years of age or older, a much higher proportion

- Dietary Approach to Stop Hypertension
  - 459 adults randomized to 3 diets
    - Control (standard American diet)
    - Diet rich in fruits and vegetables
      - But high in fat
    - DASH diet (combo diet)
      - "fruits, vegetables, and low-fat dairy products and with reduced saturated and total fat"
  - 3 week run-in diet then 8 weeks of experimental diet
  - Sodium intake and body weight were maintained constant
  - Food was provided

Hypertension: DASH Diet

TABLE 1. NUTRIENT TARGETS, MENU ANALYSES, AND AVERAGE DAILY SERVINGS OF FOODS, ACCORDING TO DIET.*

ITEM	CONTROL DIET		FRUITS-AND-VEGETABLES DIET		COMBINATION DIET	
	NUTRIENT TARGET	MENU ANALYSIS†	NUTRIENT TARGET	MENU ANALYSIS†	NUTRIENT TARGET	MENU ANALYSIS†
Nutrients						
Fat (% of total kcal)	37	35.7	37	35.7	27	25.6
Saturated	16	14.1	16	12.7	6	7.0
Monounsaturated	13	12.4	13	13.9	13	9.9
Polyunsaturated	8	6.2	8	7.3	8	6.8
Carbohydrates (% of total kcal)	48	50.5	48	49.2	55	56.5
Protein (% of total kcal)	15	13.8	15	15.1	18	17.9
Cholesterol (mg/day)	300	233	300	184	150	151
Fiber (g/day)	9	NA	31	NA	31	NA
Potassium (mg/day)	1700	1752	4700	4101	4700	4415
Magnesium (mg/day)	165	176	500	423	500	480
Calcium (mg/day)	450	443	450	534	1240	1265
Sodium (mg/day)	3000	3028	3000	2816	3000	2859
Food groups (no. of servings/day)						
Fruits and juices	1.6		5.2		5.2	
Vegetables	2.0		3.3		4.4	
Grains	8.2		6.9		7.5	
Low-fat dairy	0.1		0.0		2.0	
Regular-fat dairy	0.4		0.3		0.7	
Nuts, seeds, and legumes	0.0		0.6		0.7	
Beef, pork, and ham	1.5		1.8		0.5	
Poultry	0.8		0.4		0.6	
Fish	0.2		0.3		0.5	
Fat, oils, and salad dressing	5.8		5.3		2.5	
Snacks and sweets	4.1		1.4		0.7	

*Values are for diets designed to provide an energy level of 2100 kcal.

†Values are the results of chemical analyses of the menus prepared during the validation phase and during the trial. NA denotes not available.

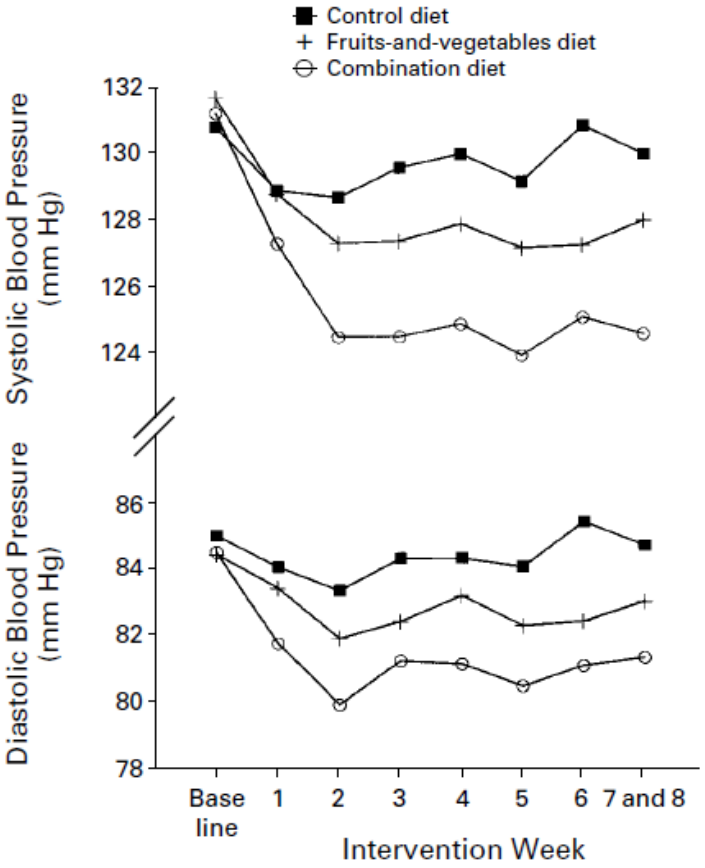
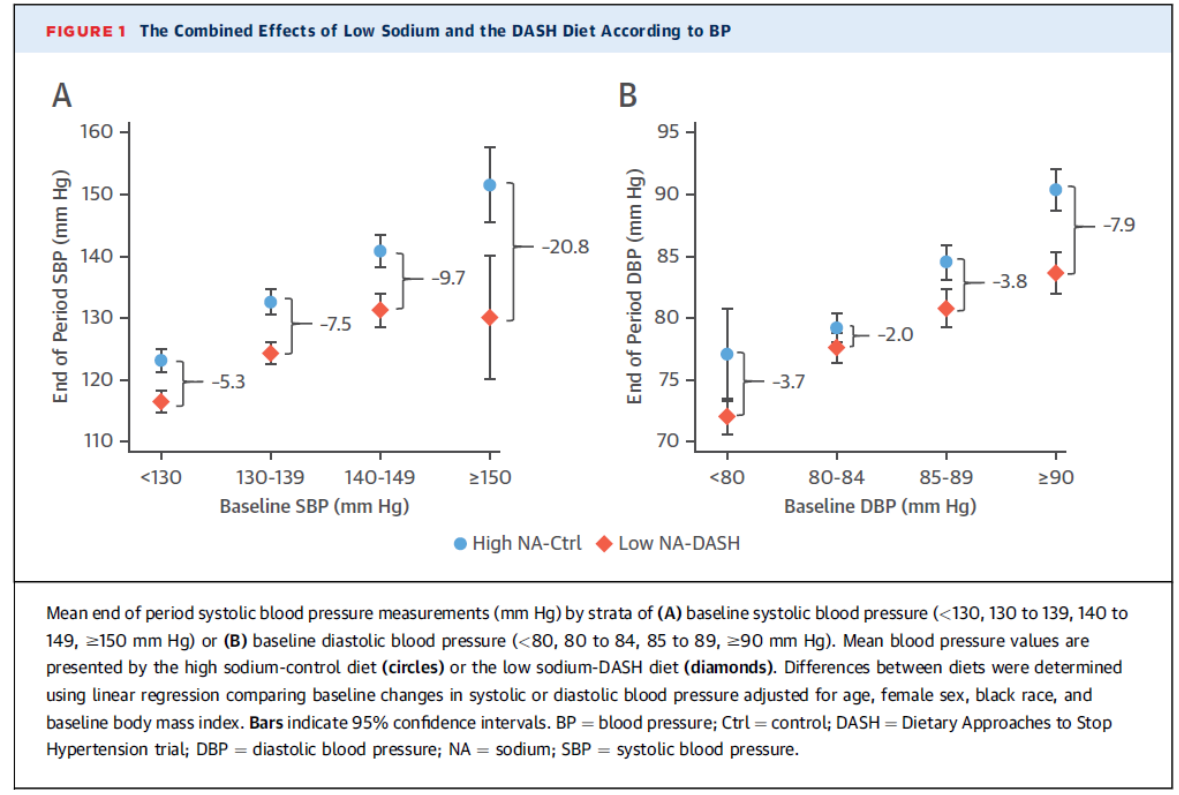


Figure 1. Mean Systolic and Diastolic Blood Pressures at Base Line and during Each Intervention Week, According to Diet, for 379 Subjects with Complete Sets of Weekly Blood-Pressure Measurements.

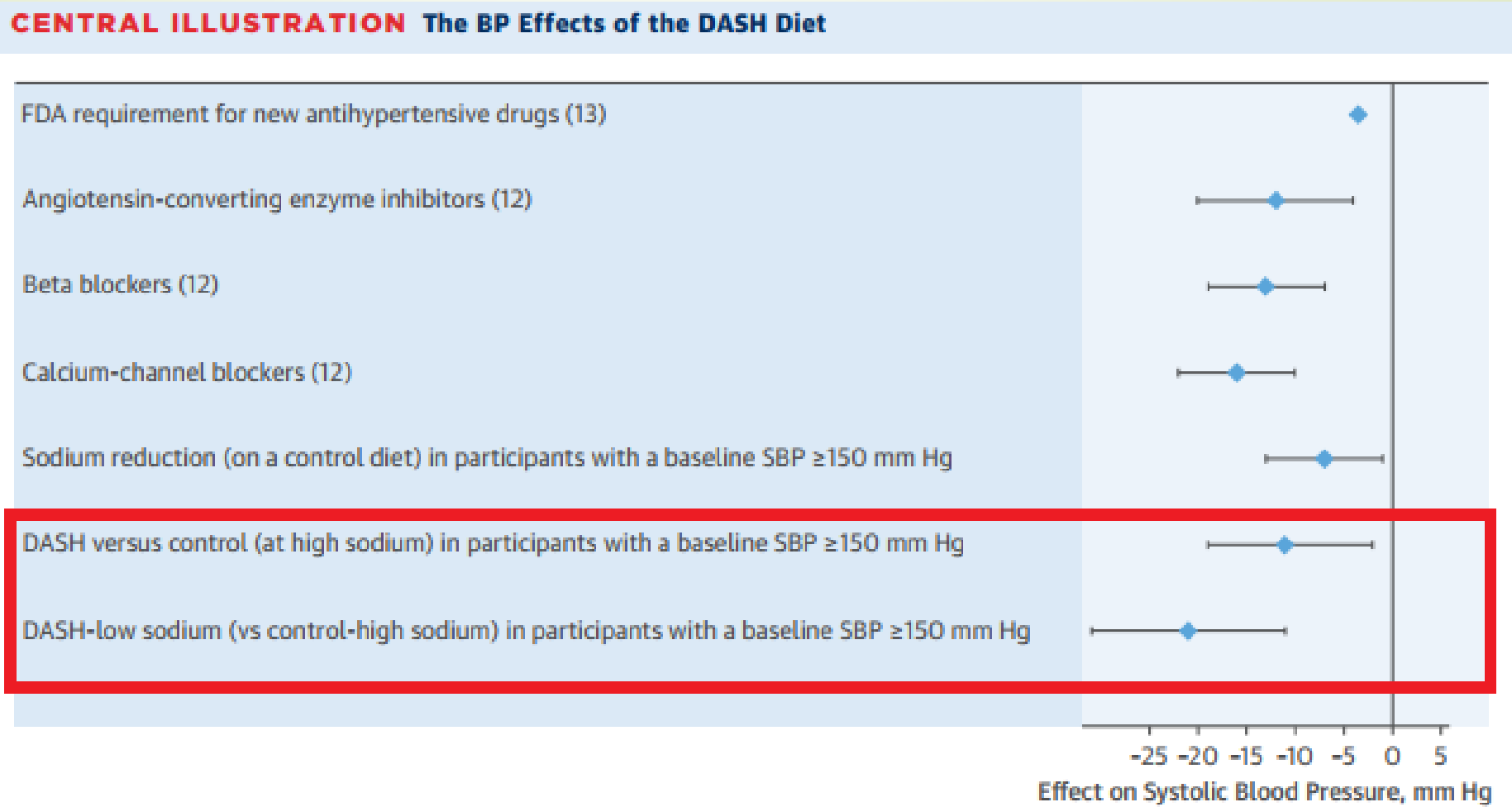
What is the maximum reduction in blood pressure with diet?



- Eating less salt and a DASH-style diet
- Blood pressure can be reduced by 21 points systolic and 8 points diastolic
- This is like going from 150/90 to 129/82

Juraschek, Stephen P., et al. "Effects of sodium reduction and the DASH diet in relation to baseline blood pressure." *Journal of the American College of Cardiology* 70.23 (2017): 2841-2848.

DASH + Low Sodium



JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

PUBLISHED BY ELSEVIER

ORIGINAL INVESTIGATIONS

Juraschek, S.P. et al. J Am Coll Cardiol. 2017;70(23):2841-8.

Effects of Sodium Reduction and the DASH Diet in Relation to Baseline Blood Pressure

Stephen P. Juraschek, MD, PhD,[a,b] Edgar R. Miller III, MD, PhD,[b] Connie M. Weaver, PhD,[c] Lawrence J. Appel, MD, MPH[b]

Can more plant foods in the diet improve this more?

Potential Mechanisms of Blood Pressure Changes

Animal Protein & Increased Blood Pressure

- Higher in sodium
- Lower in potassium
- Weight gain
- Unfavorable amino acid types
- Increased oxidative stress

Plant Protein & Reduced Blood Pressure

- Lower in sodium
- Higher in potassium
- Weight loss
- Favorable amino acid types
- Reduced oxidative stress
- Natural alkali (bicarbonate)

Joshi S, Ettinger L, Liebman S. "Plant-Based Diets and Hypertension." *American Journal of Lifestyle Medicine* 14.4 (2020): 397-405.

Effect of Food on Kidney (Plants Included)

Protein and Glomerular Filtration Rate (GFR)

	Vegans	Vegetarians	Omnivores
Protein Intake (grams/day)	82	93	112

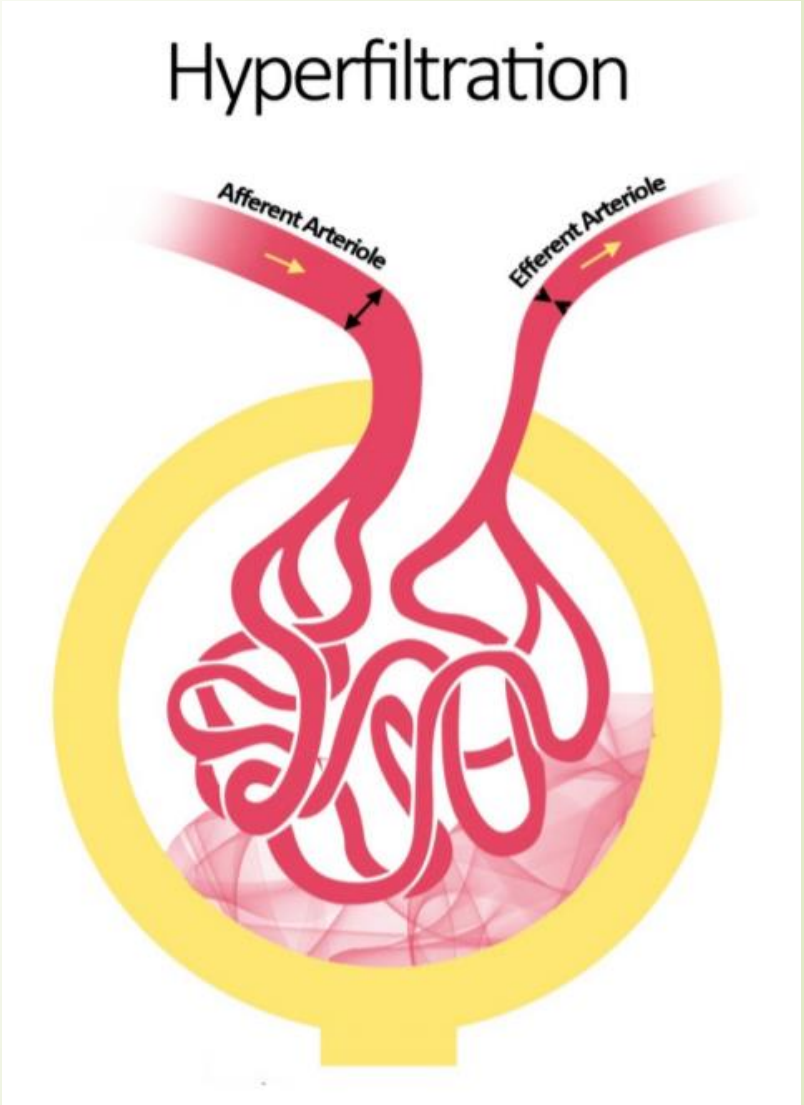
Is the additional protein harmful or harmless for the kidney?

Answer: Harmful if You Already Have Kidney Disease

Wiseman M, Hunt R, Goodwin A, Gross J, Keen H, et.al. Dietary Composition and Renal Function in healthy subjects. *Nephron*. 1987;46(1):37-42
Clarys, Peter, et al. "Comparison of nutritional quality of the vegan, vegetarian, semi-vegetarian, pesco-vegetarian and omnivorous diet." *Nutrients* 6.3 (2014): 1318-1332.

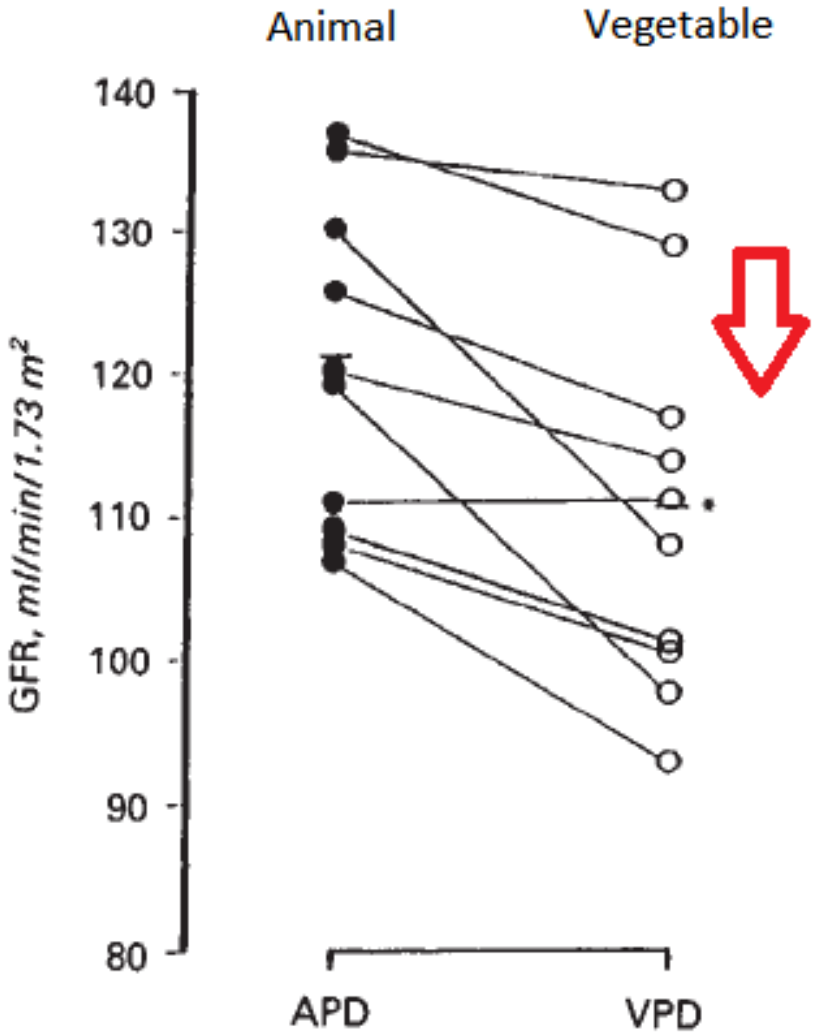
Hyperfiltration and Kidney Disease

- Additional dietary protein = hyperfiltration
- Hyperfiltration is the process of having additional blood flowing through the individual filtering units of the nephron (glomerulus)
- In damaged kidneys, this can cause even more damage
- Underlying mechanism of damage in many kidney diseases:
  - FSGS
  - Diabetes
  - Obesity
  - Cystic Kidney Disease



If excess dietary protein (in general) causes hyperfiltration, does plant protein cause less hyperfiltration?

- Only one experiment to offer any insight
- Given the same amount of protein, vegetable protein caused less hyperfiltration than animal protein
- May causes less damage in those with kidney disease
- Additionally, plant protein may have other benefits (discussed later)



Kontessis, Panayotis, et al. "Renal, metabolic and hormonal responses to ingestion of animal and vegetable proteins." *Kidney international* 38.1 (1990): 136-144.

Does animal protein increase the risk of kidney disease if you don't have kidney disease?

- Several observational studies[1,2] have shown that consumption of animal protein is associated with an increased risk of
  - Developing kidney disease
  - Developing kidney failure
  - Developing protein in the urine
- Studies have also shown similar findings in those with kidney disease as well

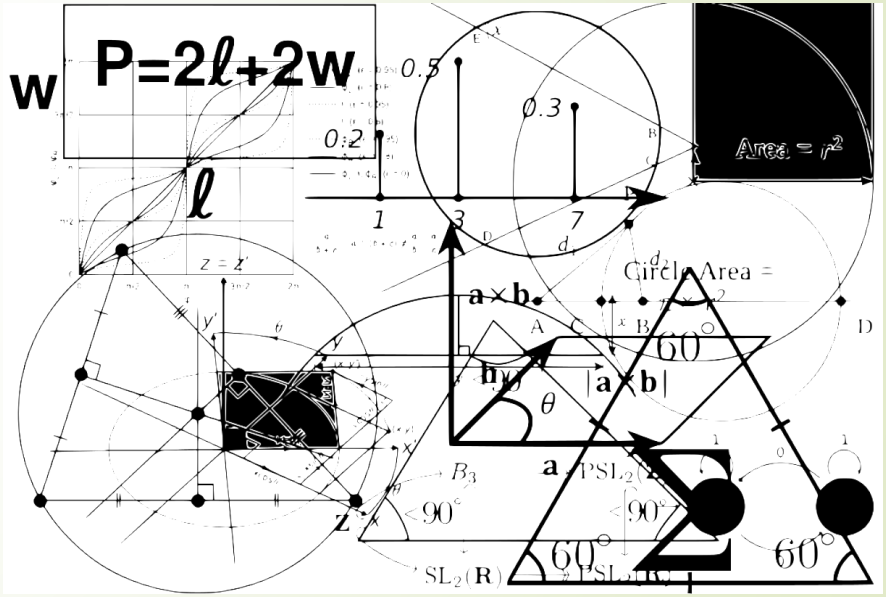
Replacing 3 % of energy from animal protein with vegetable protein lowered the prevalence ratio for the association with renal function impairment to 0.20 (95% CI: 0.06–0.63; *P* = 0.01)[3]

80% reduction in risk!

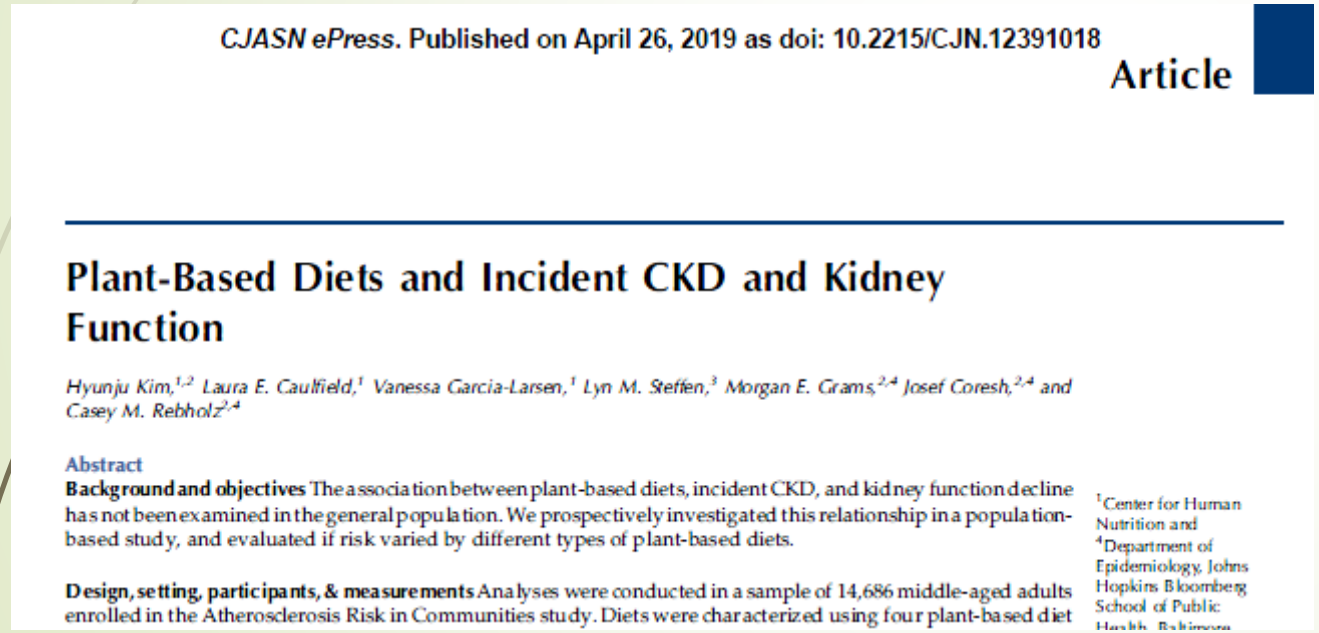
[1] Carrero et al. *Nature Reviews*. 16.9 (2020): 525-542
[2] Joshi et al. *AJKD* 77.2 (2020): 287-296
[3] Oosterwijk et al. *Kidney International Reports* 4.5 (2019): 710-719

Why might animal protein be detrimental to kidney function?

- Hyperfiltration
- Potential Renal Acid Load
- Microbiome
  - Fiber
  - TMAO
- Sodium content
- Inflammation
- Lack of Phytonutrients



Are all plant foods the same? Most definitely not…



CJASN ePress. Published on April 26, 2019 as doi: 10.2215/CJN.12391018

Article

Plant-Based Diets and Incident CKD and Kidney Function

Hyunju Kim,[1,2] Laura E. Caulfield,[1] Vanessa Garcia-Larsen,[1] Lyn M. Steffen,[3] Morgan E. Grams,[2,4] Josef Coresh,[2,4] and Casey M. Rebholz[2,4]

Abstract

Background and objectives The association between plant-based diets, incident CKD, and kidney function decline has not been examined in the general population. We prospectively investigated this relationship in a population-based study, and evaluated if risk varied by different types of plant-based diets.

Design, setting, participants, & measurements Analyses were conducted in a sample of 14,686 middle-aged adults enrolled in the Atherosclerosis Risk in Communities study. Diets were characterized using four plant-based diet

[1]Center for Human Nutrition and [4]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore

- ARIC cohort
- 14,686 adults followed for median 24 years for incident CKD
- Eating a HEALTHY plant-based diet was associated with a lower risk of CKD (highest vs lowest quintile; HR 0.85, 95% CI 0.78 to 0.96)
- Eating an UNHEALTHY plant-based diet was associated with a higher risk of CKD (highest vs lowest quintile; HR 1.11, 95% CI 1.01 to 1.24)

What foods were classified as part of a healthy plant-based diet?

Healthy & Plant-Based

- Fruits
- Vegetables
- Whole-grains
- Nuts
- Legumes
- Tea and coffee

Unhealthy/Not Plant-Based

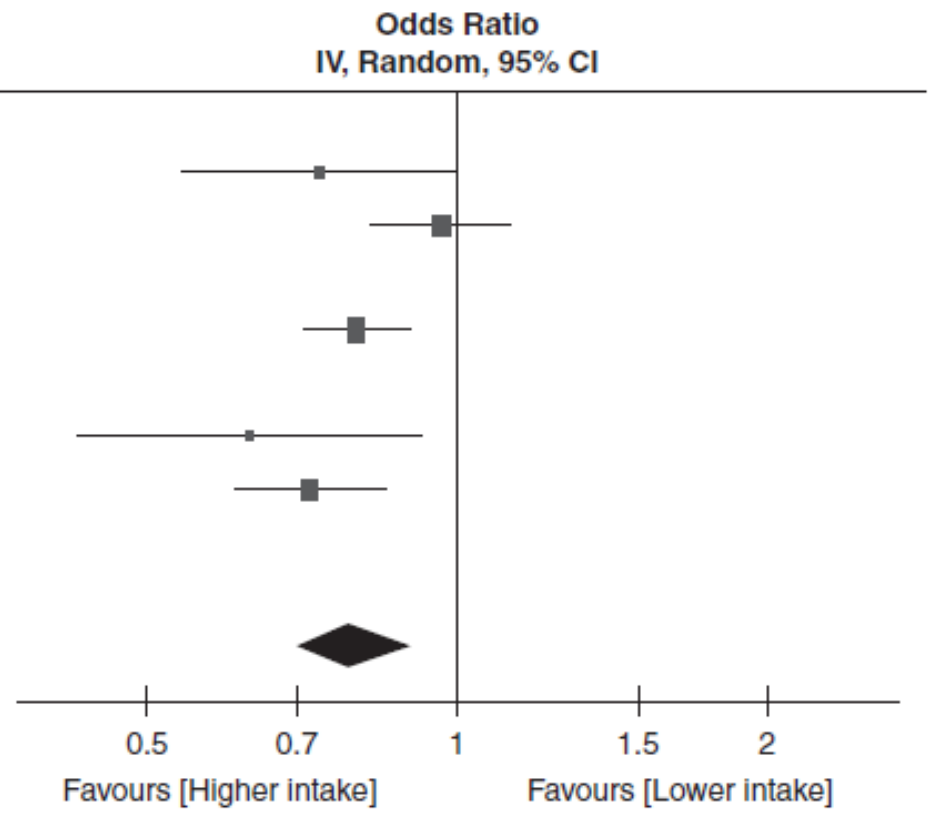
- Refined grains
- Potatoes (but definition did not separate chips & fries from baked potatoes)
- Fruit juices
- Sugar- & artificially- sweetened beverages
- Sweets and desserts
- Animal fat
- Dairy
- Meat
- Fish or seafood
- Eggs

Kim, Hyunju, et al. "Plant-Based Diets and Incident CKD and Kidney Function." *Clinical Journal of the American Society of Nephrology* (2019): CJN-12391018.

Meta-Analysis: Higher Vegetable Intake Associated with Lower Odds of Developing Kidney Disease

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Asghari 2017	-0.1744	0.3185		Not estimable
Bahadoran 2017b	-0.3064	0.1529	12.7%	0.74 [0.55, 0.99]
Dunkler 2015	-0.0336	0.0779	25.3%	0.97 [0.83, 1.13]
Haring 2017	-0.2744	0.0877		Not estimable
Jhee 2019b	-0.2231	0.0609	29.2%	0.80 [0.71, 0.90]
Mirmiran 2016	-0.462	0.1949		Not estimable
Mirmiran 2018b	-0.462	0.1949	9.0%	0.63 [0.43, 0.92]
Rebholz 2015b	-0.3285	0.0846	23.8%	0.72 [0.61, 0.85]
Rebholz 2016b	-0.0619	0.0635		Not estimable
Total (95% CI)			**100.0%**	**0.79 [0.70, 0.90]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 9.20$, df = 4 (P=0.06); $I^2 = 57\%$
Test for overall effect: Z = 3.49 (P = 0.0005)



Kelly et al. JASN 32.1(2021) 239-253

Potential Benefits of a Plant-Based Diet in Kidney Disease

Prevention of the Causes of Kidney Disease:
Type 2 Diabetes
Hypertension
Obesity

Attenuation of Kidney Disease Progression:
eGFR decline
Albuminuria

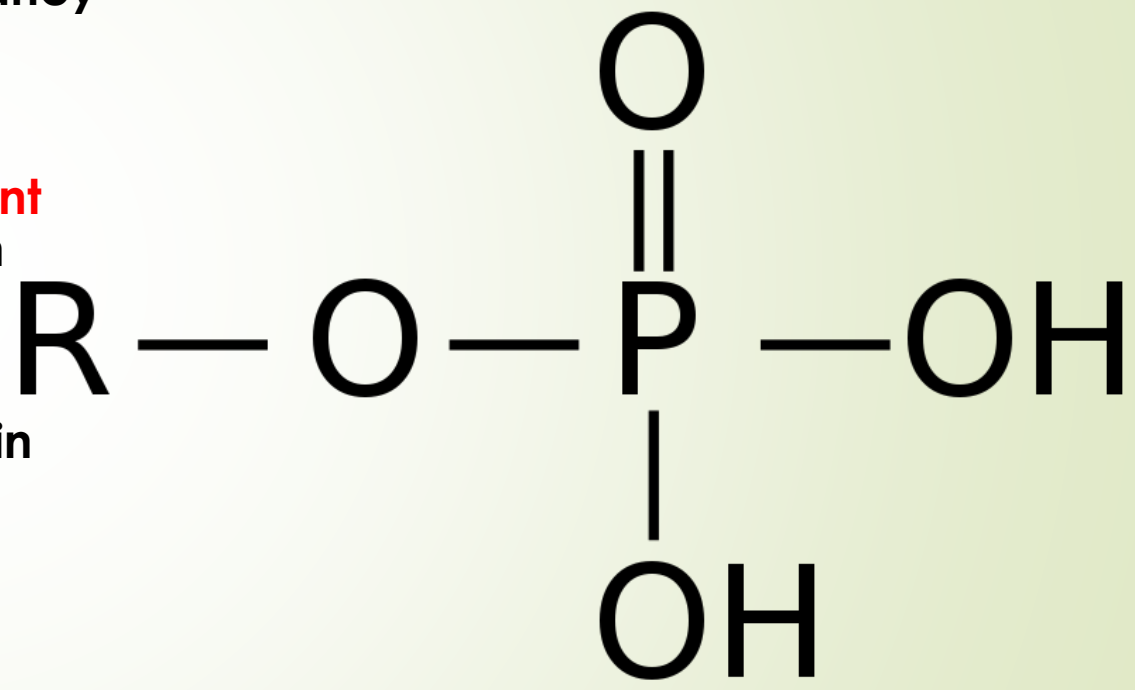
Reduction of Kidney Disease Complications:
Hyperphosphatemia
Metabolic Acidosis
Renal Hypertension
Uremic Toxins
Cardiovascular Longevity

Joshi S, McMacken M, Kalantar-Zadeh K. "Plant-Based Diets for Kidney Disease: A Guide for Clinicians." *American Journal of Kidney Diseases* 77.2 (2021): 287-296.

Hyperphosphatemia

Hyperphosphatemia

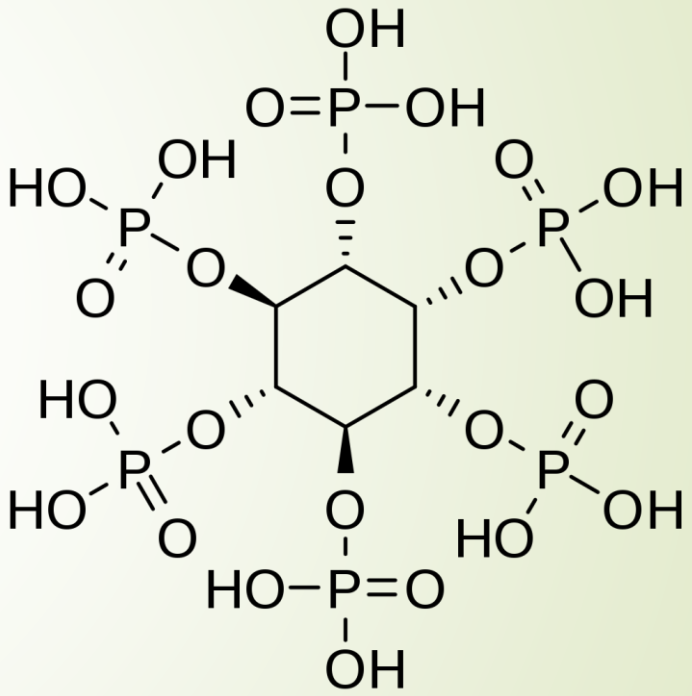
- Phosphate levels rise in advanced kidney disease
- Hyperphosphatemia is an independent risk factor for mortality in patients with CKD and ESRD[1]
- Phosphate restriction recommended in patients with CKD
  - Although adherence is difficult
  - Phosphate content not disclosed on nutrition labels!



[1]Kestenbaum, Bryan, et al. "Serum phosphate levels and mortality risk among people with chronic kidney disease." *Journal of the American Society of Nephrology* 16.2 (2005): 520-528

Dietary Sources of Phosphate

- Plant-based proteins actually have more phosphorus than animal-based proteins
  - However, plant-based phosphate is mostly bound as phytates
    - Phytates are the storage form of phosphorus in plants
    - Phosphorus in phytate form is not absorbable because humans lack the enzyme phytase



"Rule of Thirds"

Source	Serving	Phosphorus, mg	Phosphorus-Protein Ratio, mg/g	Gastrointestinal Absorption, %
Organic				
Animal protein				
Milk, skim	8 ounces	247	29	40 to 60
Yogurt, plain nonfat	8 ounces	385	27	40 to 60
Cheese, mozzarella; part skim	1 ounces	131	20	40 to 60
Egg	1 large	86	14	40 to 60
Beef (cooked)	3 ounces*	173	7	40 to 60
Chicken	3 ounces	155	8	40 to 60
Turkey	3 ounces	173	8	40 to 60
Fish, halibut	3 ounces	242	9.3	40 to 60
Fish, salmon	3 ounces	282	13.4	40 to 60
Vegetarian protein†				
Bread, whole wheat	1 slice	57	Varies	10 to 30
Bread, enriched white	1 slice	25	Varies	10 to 30
Almonds	12 ounces	134	23	10 to 30
Peanuts	1 ounce	107	15	10 to 30
Lentils (cooked)	Half a cup	178	20	10 to 30
Chocolate	1.4 ounces	142 to 216	27	10 to 30
Inorganic (additives and preservatives)‡				
Carbonated cola drink	12 ounces	40	Not Applicable	80 to 100

*A 3-ounce serving is about the size of a deck of cards.
†Phytate leads to less absorbability.
‡Inorganic phosphorous may comprise 50% or more of daily dietary phosphorus load.

Noori N, Sims JJ, Kopple JD, et al: Organic and inorganic dietary phosphorus and its management in chronic kidney disease. Iranian Journal of Kidney Diseases 4(2):89, 2010

Studies on Plant-Based Diets & Phosphorus

- Observational studies have showed:
  - that those on vegetarian diets were associated with lower serum phosphorus levels[1]
  - that those consuming lower amounts of plant protein were associated with higher urinary phosphate excretion[2]
- Interventional studies have showed:
  - that those eating 70% plant protein had lower urinary phosphate excretion[3]
  - those on a vegetarian diet had lower serum phosphorus and lower urinary phosphate excretion[4]

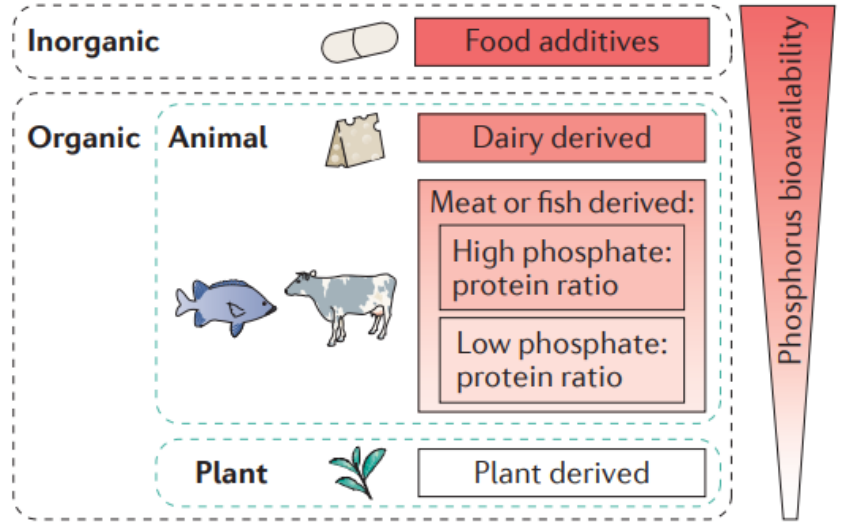


Figure 6 | **The bioavailability of phosphate differs according to the protein source.** Plant-derived phosphate has the lowest bioavailability, whereas inorganic phosphate from food additives has the highest bioavailability. Differences in the phosphate-to-protein ratio also affect the bioavailability of phosphate. Reprinted from © Adema, A.Y. *et al. J. Ren. Nutr.* **24**, 143–150 (2014), with permission from National Kidney Foundation, Inc.

[1] Wu et al. *Nephrology* (2011):582-587.
[2] Scialla et al. *Journal of Renal Nutrition* (2012):379-388.
[3] Moorthi et al. *American Journal of Nephrology* (2014):582-591.
[4] Moe et al. *CJASN* (2011):257-264.
Figure Vervloet et al. *Nat Rev Nephrol* (2017):27-38.

Big Caveat(s)!

- **Not all vegetarian diets are the same**
  - **Can vary in ratios of milk, eggs, etc**
- **Not all plants are grown under the same conditions**
  - **This can result in varying phosphorus and phytate content of plants**
- **Not all plant foods are processed in the same way**
  - **Phosphorus may be added**
  - **Different levels of processing**
- **Processing of plant foods increases the bioavailability of phosphorus**
  - **Reduces phytate binding to phosphorus**

Examples of Food Processing

- Milling
- De-hulling
- Soaking
- Germinating
- Sprouting
- Canning
- Autoclaving
- Yeast leavening
- Baking/Heating
- Extrusion

Calvo et al. Advances in Nutrition (2021): 1-12

Plant-Based Diets & Phosphorus

- Since phosphorus is not disclosed on nutrition labels and exact bioavailability is unknown, we have to estimate phosphorus absorption
- Urine recovery studies show that 51-68% of dietary phosphorus is bioavailable in lacto-ovo vegetarians
  - This is less than their omnivorous counterparts (bioavailability ranged from 60-75%)
  - Difference may be larger in vegans
- More research is needed
- In general, less phosphorus is bioavailable/absorbed in whole, unprocessed plant-foods
- Processing of legumes and grains increases phosphorus absorption
  - Soaking and rinsing is a good way to reduce phosphorus load
- Fruits and vegetables are naturally low in phosphorus

Calvo et al. Advances in Nutrition (2021): 1-12

Metabolic Acidosis

Acid in Kidney Disease

- The kidney lowers acid levels normally
- Acid levels rise in kidney disease
- Dietary proteins, especially those of animal origin, are the principal source of acid generation[1]
- Alkali has been shown to slow CKD progression[2,3]

[1]Berend. *New England Journal of Medicine* 371.15 (2014): 1434-1445.
[2]de Brito-Ashurst. *Journal of the American Society of Nephrology* 20.9 (2009): 2075-2084.
[3]Mahajan. *Kidney international* 78.3 (2010): 303-309.

Metabolic Acidosis & Diet

- Average dietary acid load is 50-75 mEq/day in America[1]
  - High in animal protein
  - Low in fruits and vegetables
- Vegan diet is nearly acid neutral[2,3]

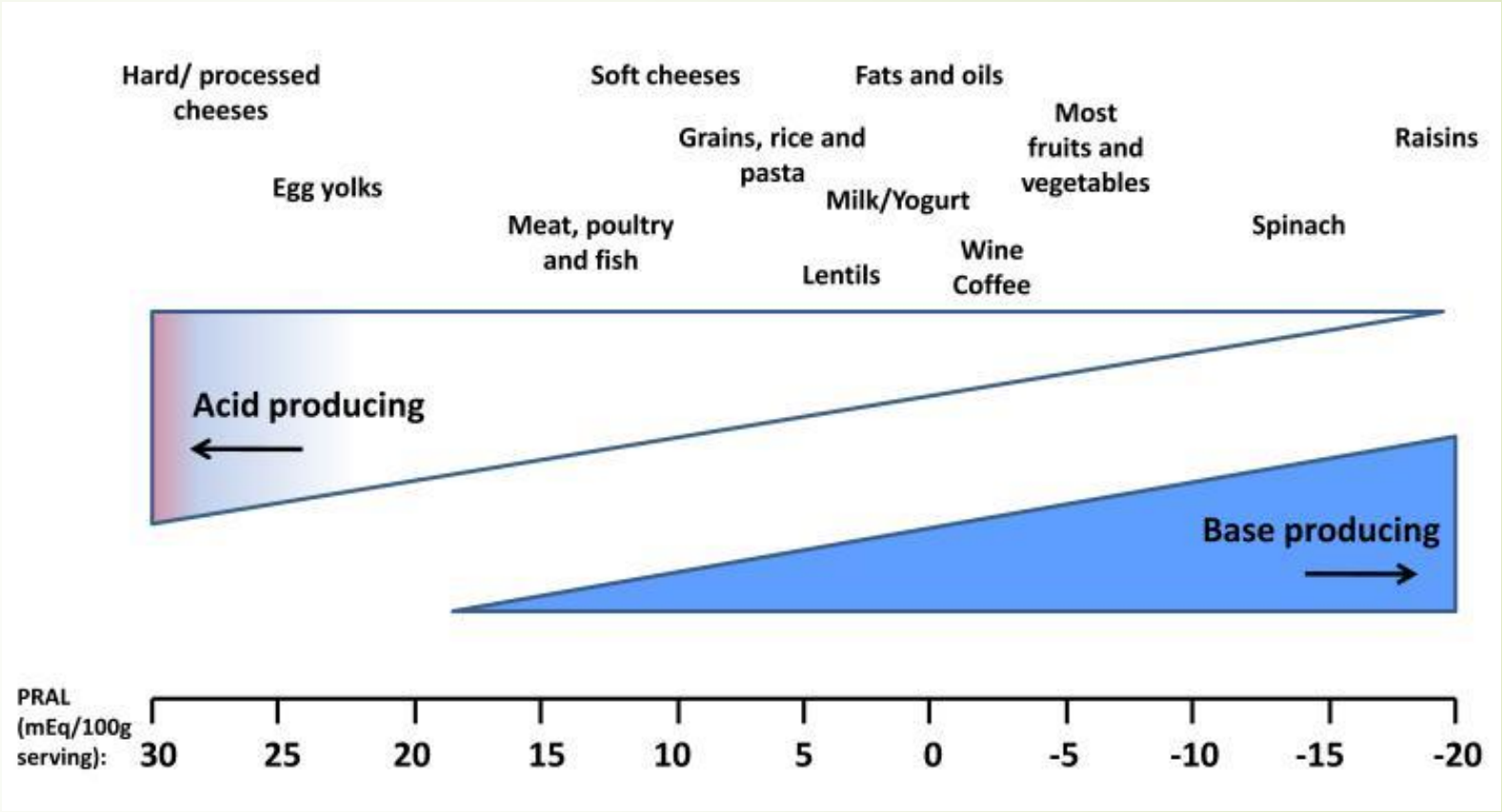


Image: Scialla, Julia J., and Cheryl AM Anderson. "Dietary acid load: a novel nutritional target in chronic kidney disease?." *Advances in chronic kidney disease* 20.2 (2013): 141-149.

[1]Ibid.

[2]Ströhle, Alexander, et al. "Diet-dependent net endogenous acid load of vegan diets in relation to food groups and bone health-related nutrients: results from the German Vegan Study." *Annals of Nutrition and Metabolism* 59.2-4 (2011): 117-126.

[3]Ausman, Lynne M., et al. "Estimated net acid excretion inversely correlates with urine pH in vegans, lacto-ovo vegetarians, and omnivores." *Journal of Renal Nutrition* 18.5 (2008): 456-465.

Fruits and Vegetables for Metabolic Acidosis

- Current treatment = baking soda (sodium bicarbonate)
- Several randomized, controlled trials have shown that 2-4 cups of fruits and vegetables are just as effective[1-3]
  - Fruits and vegetables have natural alkali (like citrate, malate, and bicarbonate)
  - CKD Stages I-V
- Fruits and vegetables actually were better than baking soda for
  - Weight loss[1-3]
  - Blood pressure[1-3]
  - Urine protein[1,3]
- No increase in potassium levels[1-3]

[1] Goraya. *Kidney International* 81.1 (2012): 86-93.
[2] Goraya. *Kidney International* 86.5 (2014): 1031-1038.
[3] Goraya. *CJASN* 8.3 (2013): 371-381.

Fruits and Vegetables or Sodium Bicarbonate?

http://www.kidney-international.org

see original article on page 86

The key to halting progression of CKD might be in the produce market, not in the pharmacy

Jaime Uribarri[1] and Man S. Oh[2]

In vitro, experimental, and clinical work suggests that metabolic acidosis, either directly or indirectly, can promote the progression of chronic kidney disease (CKD). Goraya *et al.* demonstrate that both oral alkali supplementation and a diet rich in fruits and vegetables are

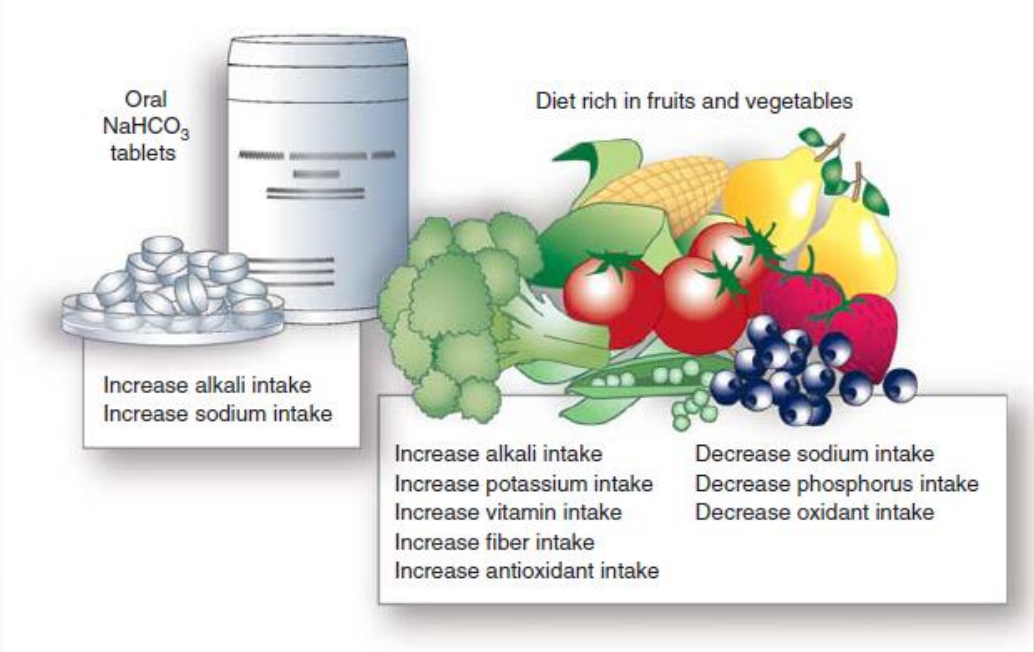
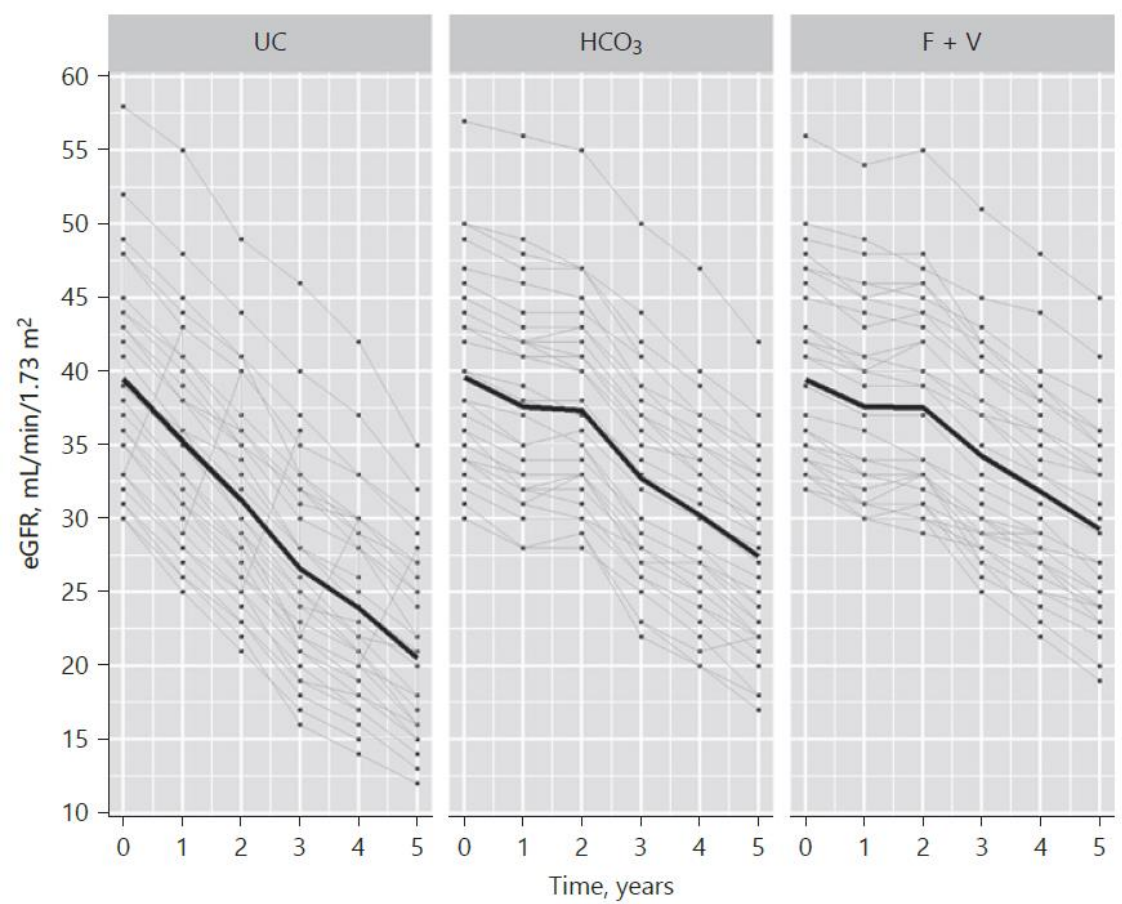


Figure 1 | Alkali supplementation in CKD: $NaHCO_3$ or a diet rich in fruits and vegetables?

5-year RCT: Alkali Therapy Slows GFR Loss



Fruits that were provided predominantly were apples, apricots, oranges, peaches, pears, raisins, and strawberries. Vegetables that were provided predominantly were carrots, cauliflower, eggplant, lettuce, potatoes, spinach, tomatoes, and zucchini.

- Alkali therapy slowed loss of GFR over five years
- Both fruits and vegetables and sodium bicarbonate supplementation were equivalent in slowing GFR loss
- Those eating fruits and vegetables also had significantly lower blood pressures
  - Lower weight (4 kg; compared to start of intervention)
  - Lower BPs (~ 8 mm Hg; compared to $HCO3^-$ group)
- No hyperkalemia

Goraya *et al*. *American Journal of Nephrology* 49.6 (2019): 438-448.

Mortality

Mortality in Kidney Disease

- Kidney disease is extremely deadly
- Those with kidney disease are **16 to 40 times more likely** to die than to progress to kidney failure[1] (might be an underestimate?)
- Those with kidney failure don't fair any better
  - 5-year survival rate is 42%[2]
    - This is worse than early stage lung cancer

[1] https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=34
[2] https://www.usrds.org/2018/view/v2_05.aspx

Some Mortality Estimates of Patient with ESRD are Even Higher

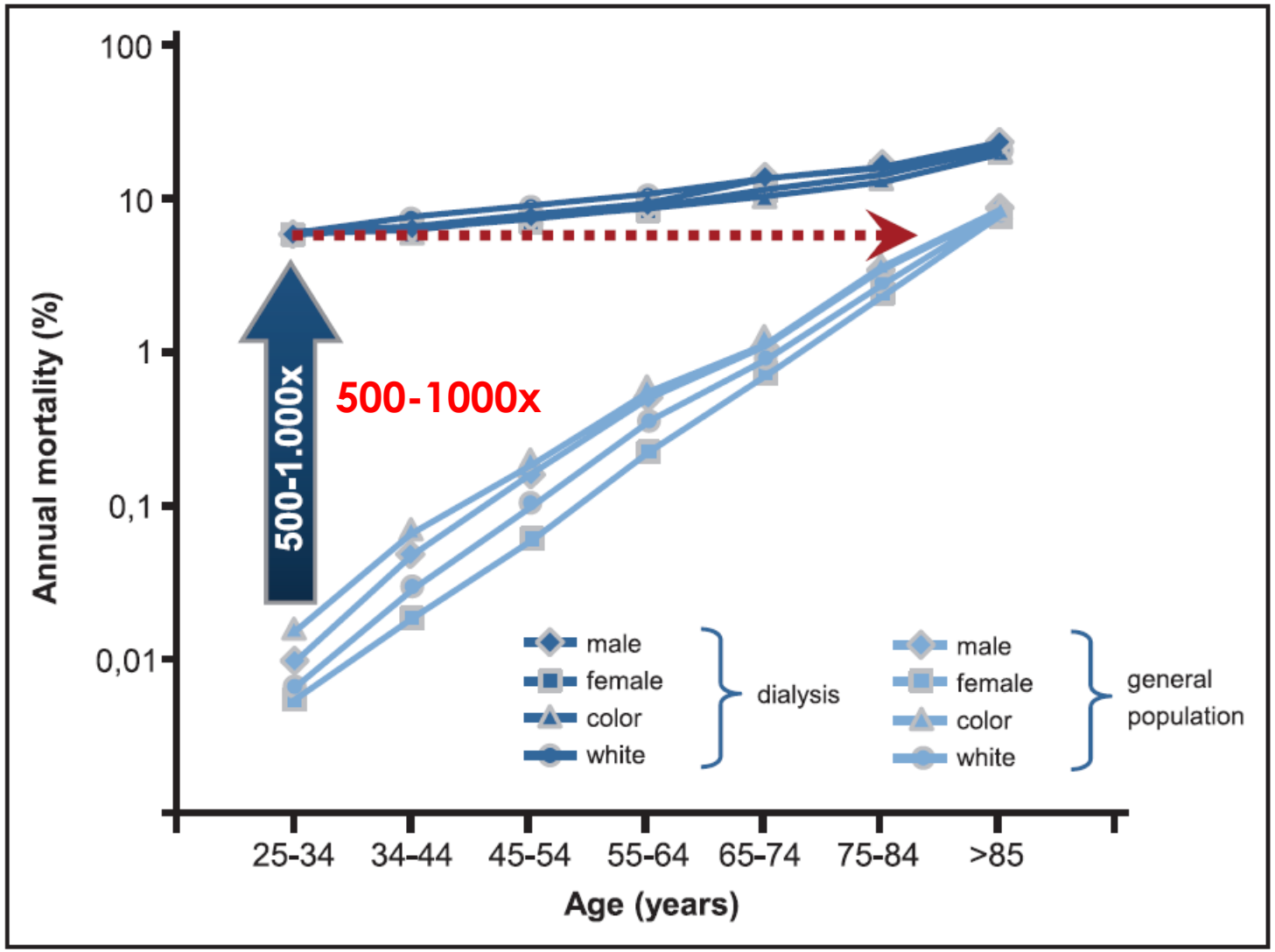


Figure 1. Cardiovascular mortality in the general population and in patients with end-stage kidney disease.
In 25- to 34-year-old patients with end-stage kidney disease, annual mortality is increased 500- to 1000-fold and corresponds to that of the ≈85-year-old general population. Adapted from Foley et al.[5]

Jankowski et al. *Circulation* 143.11 (2021): 1157-1172.

Plant-Based Diets in CKD & Mortality

Article

Healthy Dietary Patterns and Risk of Mortality and ESRD in CKD: A Meta-Analysis of Cohort Studies

Jaimon T. Kelly, Suetonia C. Palmer,† Shu Ning Wai,* Marinella Ruospo,‡§ Juan-Jesus Carrero,‖ Katrina L. Campbell,* and Giovanni F. M. Strippoli§¶***

Abstract

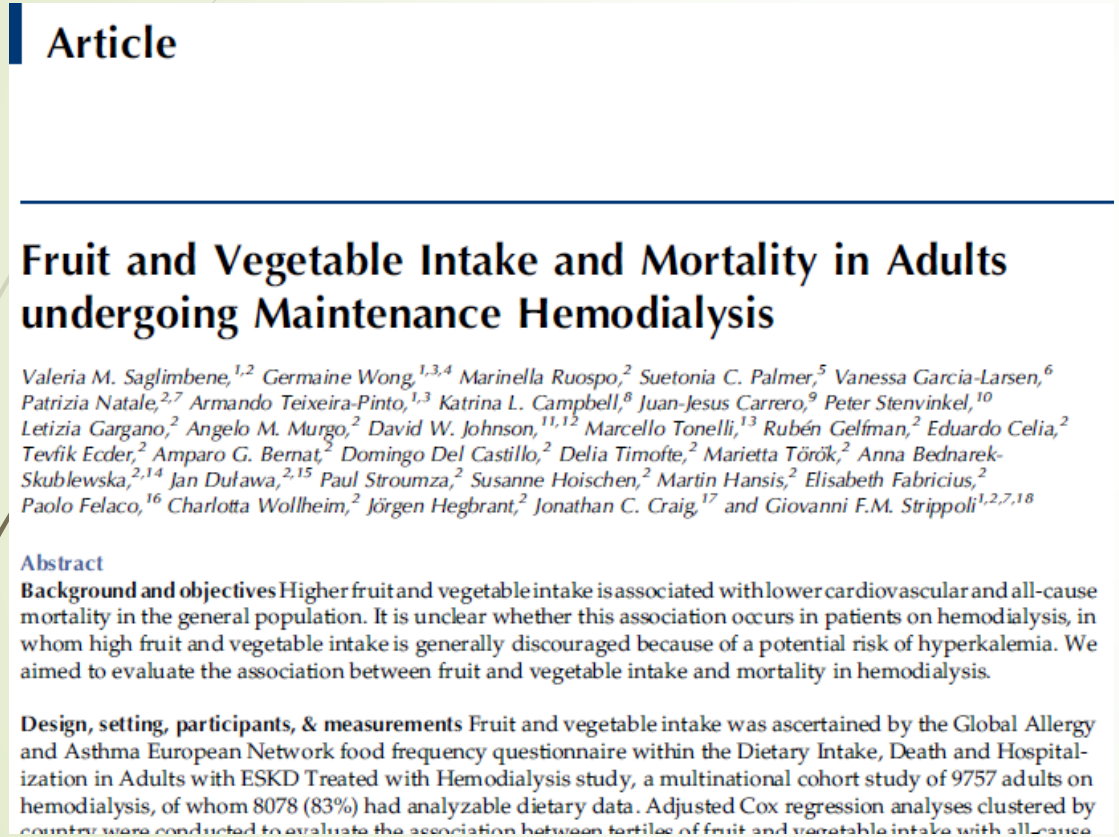
Background and objectives Patients with CKD are advised to follow dietary recommendations that restrict individual nutrients. Emerging evidence indicates overall eating patterns may better predict clinical outcomes, however, current data on dietary patterns in kidney disease are limited.

Design, setting, participants, & measurements This systematic review aimed to evaluate the association between dietary patterns and mortality or ESRD among adults with CKD. Medline, Embase, and reference lists were systematically searched up to November 24, 2015 by two independent review authors. Eligible studies were longitudinal cohort studies reporting the association of dietary patterns with mortality, cardiovascular events, or ESRD.

Results A total of seven studies involving 15,285 participants were included. Healthy dietary patterns were generally higher in fruit and vegetables, fish, legumes, cereals, whole grains, and fiber, and lower in red meat, salt, and refined sugars. In six studies, healthy dietary patterns were consistently associated with lower mortality (3983 events; adjusted relative risk, 0.73; 95% confidence interval, 0.63 to 0.83; risk difference of 46 fewer (29–63

- Meta-Analysis of 6 prospective cohort studies including nearly 14,000 adults with CKD
- Eating a healthy dietary pattern associated with a lower risk of mortality (adjusted relative risk 0.73, 95% CI 0.63-0.83)
- More fruits, vegetables, fish, legumes, cereals, whole grains, fiber AND less red meat, salt, and refined sugars

Plant-Based Diets in ESRD & Mortality



Article

Fruit and Vegetable Intake and Mortality in Adults undergoing Maintenance Hemodialysis

Valeria M. Saglimbene,[1,2] Germaine Wong,[1,3,4] Marinella Ruospo,[2] Suetonia C. Palmer,[5] Vanessa Garcia-Larsen,[6] Patrizia Natale,[2,7] Armando Teixeira-Pinto,[1,3] Katrina L. Campbell,[8] Juan-Jesus Carrero,[9] Peter Stenvinkel,[10] Letizia Gargano,[2] Angelo M. Murgo,[2] David W. Johnson,[11,12] Marcello Tonelli,[13] Rubén Gelfman,[2] Eduardo Celia,[2] Tevfik Ecder,[2] Amparo G. Bernat,[2] Domingo Del Castillo,[2] Delia Timofte,[2] Marietta Török,[2] Anna Bednarek-Skublewska,[2,14] Jan Duława,[2,15] Paul Stroumza,[2] Susanne Hoischen,[2] Martin Hansis,[2] Elisabeth Fabricius,[2] Paolo Felaco,[16] Charlotta Wollheim,[2] Jörgen Hegbrant,[2] Jonathan C. Craig,[17] and Giovanni F.M. Strippoli[1,2,7,18]

Abstract

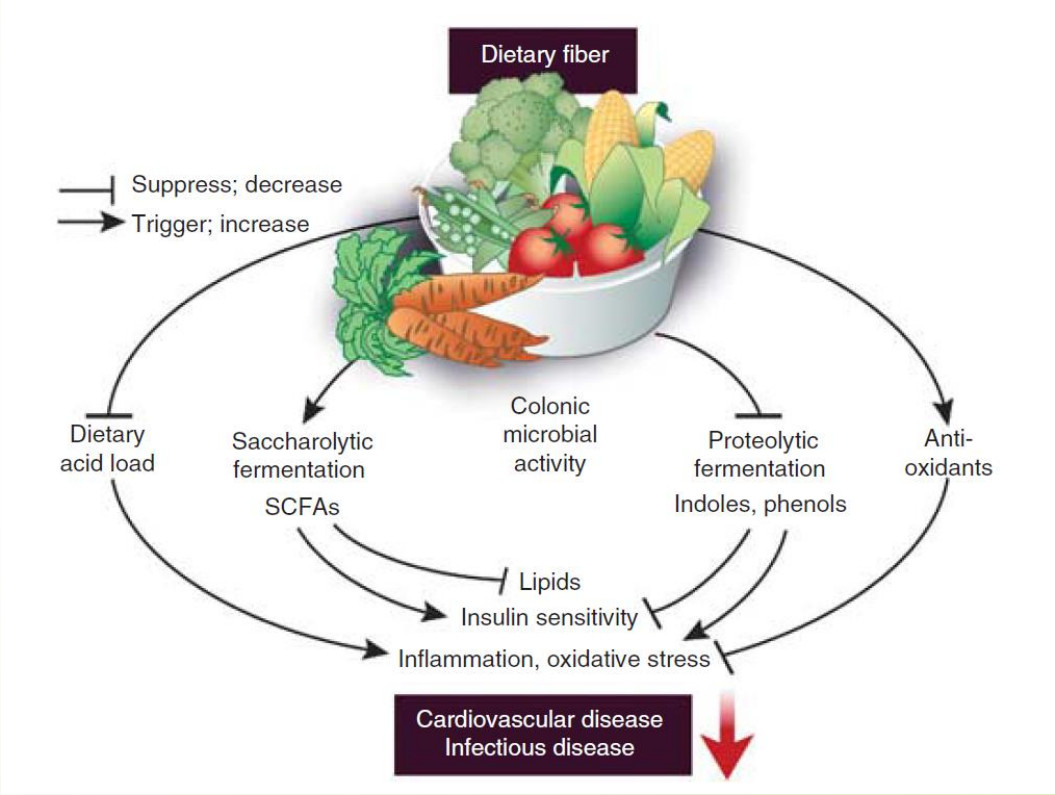
Background and objectives Higher fruit and vegetable intake is associated with lower cardiovascular and all-cause mortality in the general population. It is unclear whether this association occurs in patients on hemodialysis, in whom high fruit and vegetable intake is generally discouraged because of a potential risk of hyperkalemia. We aimed to evaluate the association between fruit and vegetable intake and mortality in hemodialysis.

Design, setting, participants, & measurements Fruit and vegetable intake was ascertained by the Global Allergy and Asthma European Network food frequency questionnaire within the Dietary Intake, Death and Hospitalization in Adults with ESKD Treated with Hemodialysis study, a multinational cohort study of 9757 adults on hemodialysis, of whom 8078 (83%) had analyzable dietary data. Adjusted Cox regression analyses clustered by country were conducted to evaluate the association between tertiles of fruit and vegetable intake with all-cause

- Prospective study from DIET-HD cohort involving 11 countries in Europe and South America
- Approx. 8,000 people followed for a median of 2.7 years
- Fruit and Vegetable (F+V) intake and mortality were measured
- Median number of servings was 8 per week
- Only 4% consumed 4 servings per day (the recommended minimum)
- Compared with the lowest tertile of servings per week, those in the highest tertile were associated with a lower risk of all-cause mortality (HR 0.80, 95% CI 0.71 – 0.91) and non-CV mortality (HR 0.77, 95% CI 0.66 – 0.91)

Fiber Associated with Reduced Mortality in Kidney Disease

- **Dietary fiber was used as a treatment for kidney failure 40 years ago because it reduced blood levels of nitrogenous waste (urea)[1]**
- **Fiber intake has been associated with reduced mortality and cardiovascular disease in CKD[2,3]**
- **In one study, every extra 1 gram of fiber was associated with an 11% reduction in cardiovascular events[3]**



[1] Rose et al. Uro & Nephron. 2019; 6(3): 555687
[2] Evenepoel. *Kidney International* 81.3 (2012): 227-229.
[3] Wang. *Kidney International Reports* 4.6 (2019): 814-823.
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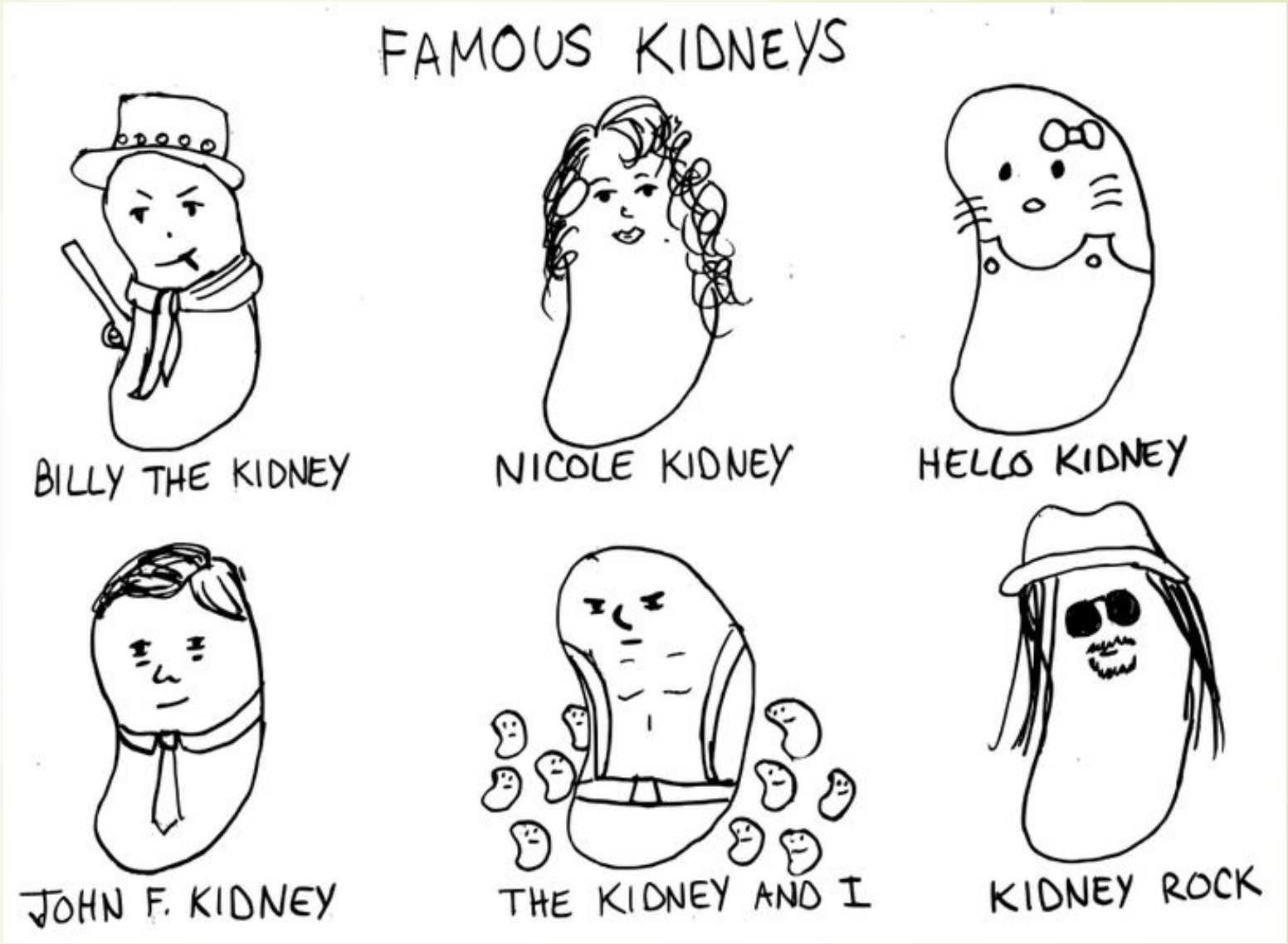
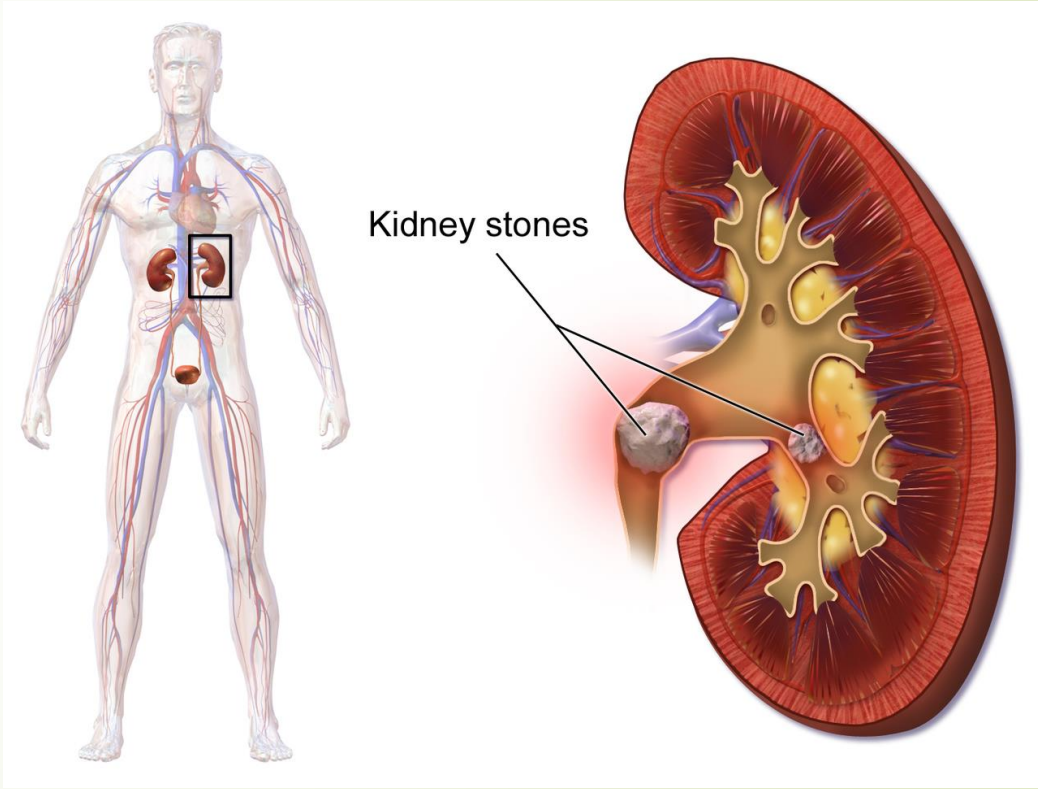

FAMOUS KIDNEYS
BILLY THE KIDNEY
NICOLE KIDNEY
HELLO KIDNEY
JOHN F. KIDNEY
THE KIDNEY AND I
KIDNEY ROCK

Kidney Stones

Kidney Stones

- Prevalence of kidney stones is ~10%
  - Prevalence is increasing
- Most common stone is a calcium oxalate stone[2]
  - 70 to 80% of stones are comprised of calcium oxalate[1]
- Risk of recurrence is 40% at 5 years and 75% at 20 years[2]



[1] Abufaraj, Mohammad, et al. "Prevalence and Trends in Kidney Stone Among Adults in the USA: Analyses of National Health and Nutrition Examination Survey 2007–2018 Data." *European Urology Focus* (2020).

[2] Worcester, Elaine M., and Fredric L. Coe. "Calcium kidney stones." *New England Journal of Medicine* 363.10 (2010): 954-963.

Stones & Animal Protein

Robust evidence linking animal protein and stone formation dating back to the end of WWII

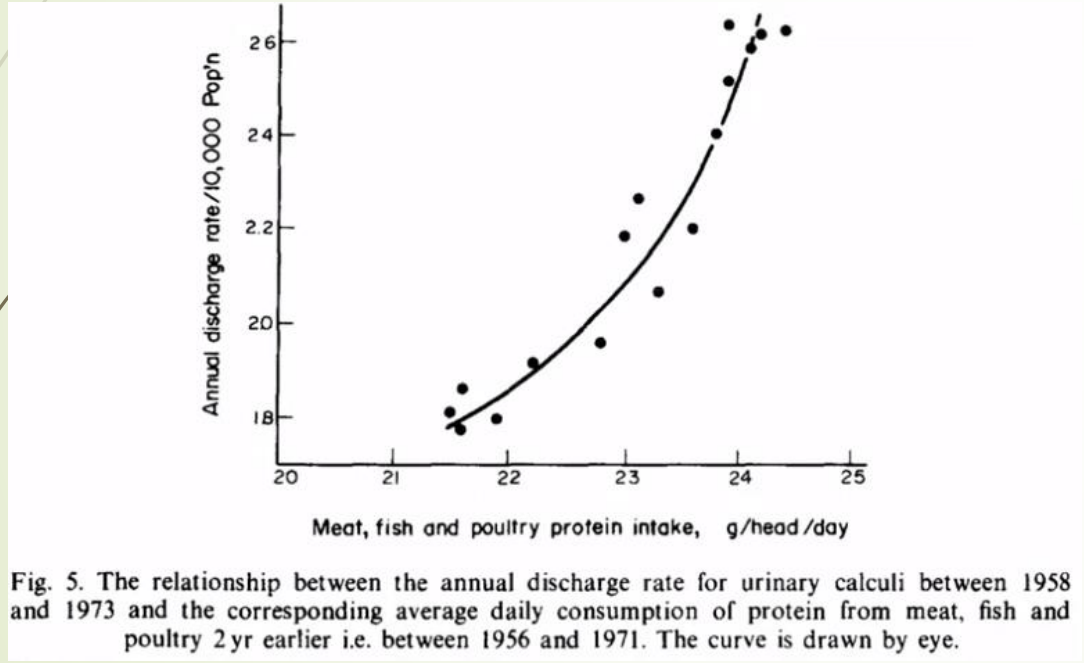


Fig. 5. The relationship between the annual discharge rate for urinary calculi between 1958 and 1973 and the corresponding average daily consumption of protein from meat, fish and poultry 2 yr earlier i.e. between 1956 and 1971. The curve is drawn by eye.

Figure: Robertson, W. G., M. Peacock, and A. Hodgkinson. "Dietary changes and the incidence of urinary calculi in the UK between 1958 and 1976." *Journal of Chronic Diseases* 32.6 (1979): 469-476.

Should Recurrent Calcium Oxalate Stone formers become Vegetarians?

W. G. ROBERTSON, M. PEACOCK, P. J. HEYBURN, F. A. HANES, A. RUTHERFORD, E. CLEMENTSON, R. SWAMINATHAN and P. B. CLARK

MRC Mineral Metabolism Unit, Department of Chemical Pathology and Department of Urology, General Infirmary, Leeds

Summary—The hypothesis that the incidence of calcium stone disease is related to the consumption of animal protein has been examined. Within the male population, recurrent idiopathic stone formers consumed more animal protein than did normal subjects. Single stone formers had animal protein intakes intermediate between those of normal men and those of recurrent stone formers.

A high animal protein intake caused a significant increase in the urinary excretion of calcium, oxalate and uric acid, 3 of the 6 main urinary risk factors for calcium stone formation. The overall relative probability of forming stones, calculated from the combination of the 6 main

Robertson, W. G., et al. "Should recurrent calcium oxalate stone formers become vegetarians?." *BJU International* 51.6 (1979): 427-431.

Stones & Animal Protein

- **"Stone formers should be advised to limit the intake of all animal proteins, including fish"[1]**
- **Animal protein consumption raises urinary levels of**
  - **Calcium**
  - **Oxalate**
  - **Uric Acid**
  - **Acidity**

  All increase stone risk
- **"For calcium oxalate stone formers, treatment is animal-protein and sodium restriction NOT calcium restriction"[2]**

[1] Tracy, Chad R., et al. "Animal protein and the risk of kidney stones: a comparative metabolic study of animal protein sources." *The Journal of urology* 192.1 (2014): 137-141.
[2] Borghi, Loris, et al. "Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria." *New England Journal of Medicine* 346.2 (2002): 77-84.

Vegetarians Associated with a Lower Risk of Kidney Stones

Eur Urol. 1982;8(6):334-9.

Prevalence of urinary stone disease in vegetarians.

Robertson WG, Peacock M, Marshall DH.

Abstract

A study was carried out to determine the effect of a low animal protein diet, su
disease. A nation-wide survey of vegetarians in the UK showed that the preva
a group of individuals taken from the general population and matched for age,
the hypothesis that a diet low in animal protein reduces the risk of urinary stor

PMID: 7140784

[Indexed for MEDLINE]

Eur J Epidemiol. 2014 May;29(5):363-9. doi: 10.1007/s10654-014-9904-5. Epub 2014 Apr 22.

Diet and risk of kidney stones in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC).

Turney BW[1], Appleby PN, Reynard JM, Noble JG, Key TJ, Allen NE.

Author information

Abstract

The lifetime prevalence of kidney stones is around 10 % and incidence rates are increasing. Diet may be an important determinant of kidney stone development. Our objective was to investigate the association between diet and kidney stone risk in a population with a wide range of diets. This association was examined among 51,336 participants in the Oxford arm of the European Prospective Investigation into Cancer and Nutrition using data from Hospital Episode Statistics in England and Scottish Morbidity Records. In the cohort, 303 participants attended hospital with a new kidney stone episode. Cox proportional hazards regression was performed to calculate hazard ratios (HR) and their 95 % confidence intervals (95 % CI). Compared to those with high intake of meat (>100 g/day), the HR estimates for moderate meat-eaters (50-99 g/day), low meat-eaters (<50 g/day), fish-eaters and vegetarians were 0.80 (95 % CI 0.57-1.11), 0.52 (95 % CI 0.35-0.8), 0.73 (95 % CI 0.48-1.11) and 0.69 (95 % CI 0.48-0.98), respectively. High intakes of fresh fruit, fibre from wholegrain cereals and magnesium were also associated with a lower risk of kidney stone formation. A high intake of zinc was associated with a higher risk. In conclusion, vegetarians have a lower risk of developing kidney stones compared with those who eat a high meat diet. This information may be important to advise the public about prevention of kidney stone formation.

PMID: 24752465 DOI: 10.1007/s10654-014-9904-5

[Indexed for MEDLINE]

Vegetarians Have a Lower Risk of Kidney Stones

Factor and category	Median for men	Median for women	All participants			*p* value for trend
			N	HR	95 % CI	
Diet group and intake of meat (g/day)						
Meat 100+	135	127	72	1.00		
Meat 50–99	74	74	74	0.80	0.57–1.11	
Meat <50	30	28	35	0.52	0.35–0.80	
Fish eater	0	0	38	0.73	0.48–1.11	
Vegetarian	0	0	84	0.69	0.48–0.98	0.04
Total meat and meat products (g/day)[a]						
Bottom	34.6	28.1	41	1.00		
Middle	78.0	69.4	65	1.50	1.00–2.23	
Top	135.1	118.5	75	1.64	1.08–2.48	0.04

- **Prospective Cohort from EPIC (European Prospective Investigation into Cancer and Nutrition)**
- **51,336 people from England & Scotland**
- **Vegetarians associated with 31% risk reduction in kidney stone formation**
- **Top tertile of meat eaters associated with a 64% increased risk in kidney stone formation**

Turney, Benjamin W., et al. "Diet and risk of kidney stones in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC)." *European Journal of Epidemiology* 29.5 (2014): 363-369.

Stones & Plant Protein

- **Fruits and vegetables reduce risk of kidney stones (despite having purines) via[1]**
  - **Lower urine acidity**
  - **Lower urine uric acid**
  - **Lower urine calcium excretion**
  - **Lower sodium excretion**
  - **Increases urine citrate**

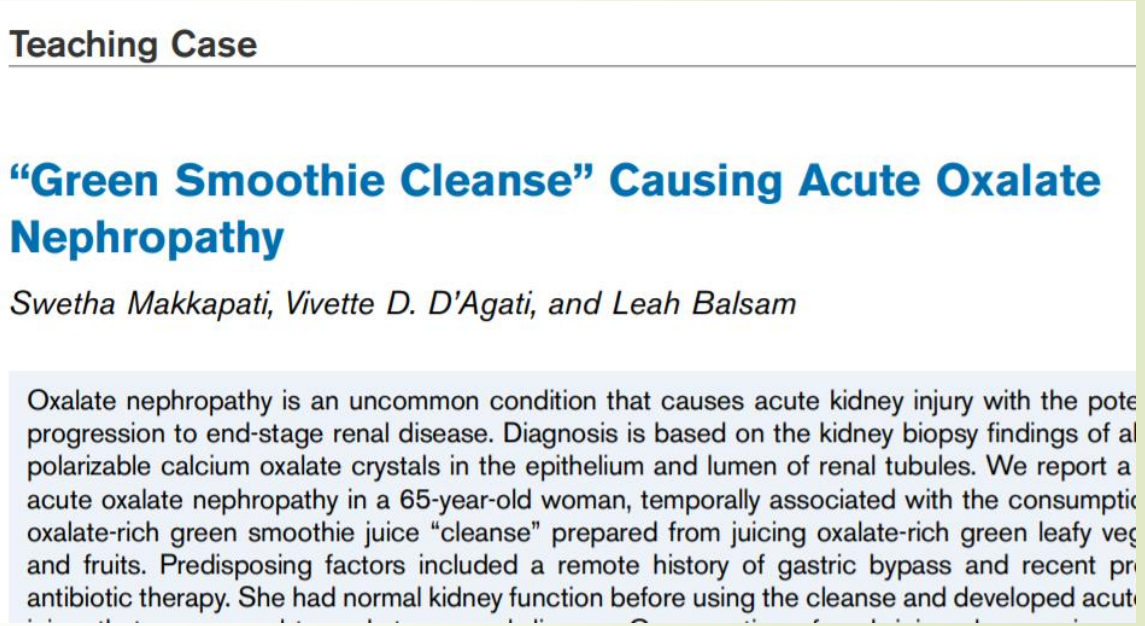
- **Potassium citrate is commonly prescribed for calcium oxalate stones because "because an alkaline ash diet is difficult to follow for most patients"[2]**
- **Potassium citrate**
  - **Potassium = found in fruits and vegetables**
  - **Citrate = found in fruits and vegetables**

[1]Sorensen, Mathew D., et al. "Dietary intake of fiber, fruit and vegetables decreases the risk of incident kidney stones in women: a Women's Health Initiative report." *The Journal of urology* 192.6 (2014): 1694-1699.

[2]Han, Haewook, et al. "Nutritional management of kidney stones (nephrolithiasis)." *Clinical nutrition research* 4.3 (2015): 137-152.

But what about all those oxalates in plant foods?

- **Oxalate is compound found naturally in plants to bind calcium** (thought to facilitate growth of plants in areas of high calcium levels in the soil)
- **Some extremely high oxalate-containing foods, if consumed frequently, can lead to a calcium stone**
  - Spinach, swiss chard, beet greens, rhubarb, cashews, starfruit, dark chocolate, potatoes, black tea



Teaching Case

"Green Smoothie Cleanse" Causing Acute Oxalate Nephropathy

Swetha Makkapati, Vivette D. D'Agati, and Leah Balsam

Oxalate nephropathy is an uncommon condition that causes acute kidney injury with the pote
progression to end-stage renal disease. Diagnosis is based on the kidney biopsy findings of al
polarizable calcium oxalate crystals in the epithelium and lumen of renal tubules. We report a
acute oxalate nephropathy in a 65-year-old woman, temporally associated with the consumptio
oxalate-rich green smoothie juice "cleanse" prepared from juicing oxalate-rich green leafy veg
and fruits. Predisposing factors included a remote history of gastric bypass and recent pr
antibiotic therapy. She had normal kidney function before using the cleanse and developed acut

However, Only Select Patients Needs to Restrict Oxalates

- Dietary oxalate restriction results in a trivial reduction on urinary oxalate excretion in the average person[1,2]
  - Absorption is variable depending on solubility of oxalate and the levels of binding of dietary calcium
  - Increased dietary oxalate consumption fosters growth of colonic bacteria (*Oxalobacter formigenes*) that digest oxalate
- Patients with chronic hyperoxaluria should be monitored under the supervision of a nephrologist with
  - Periodic 24 hour urine collections for stone-risk
  - Recommendation to avoid ultra-high oxalate foods (spinach, swiss chard, beet greens, rhubarb, cashews, starfruit, etc.)
- Other risk factors for hyperoxaluria: bowel disease, bowel surgery, antibiotics, vitamin C supplementation

[1] Marvin Grieff, David A. Bushinsky. "Chapter 42 - Nutritional Prevention and Treatment of Kidney Stones." Editor(s): Joel D. Kopple, Shaul G. Massry, Kamyar Kalantar-Zadeh, Nutritional Management of Renal Disease, Academic Press, 2013, Pages 699-709, ISBN 9780123919342, https://doi.org/10.1016/B978-0-12-391934-2.00042-4.
[2] Taylor, Eric N., and Gary C. Curhan. "Determinants of 24-hour urinary oxalate excretion." *Clinical Journal of the American Society of Nephrology* 3.5 (2008): 1453-1460.

Risks of Plant-Based Diets in Kidney Disease

Potassium

Plant-Based Foods, Potassium, and CKD

- Historically, plant-based foods have been excluded from "renal diets" due to their potassium content
- However, recent research suggests that this risk may be overstated
- Factors mitigating a rise in serum potassium in CKD with plant-based foods:
  - **Fiber** – Leads to larger and more frequent bowel movements, leading to potassium loss
  - **Colonic Secretion of Potassium** – In CKD, **up to 30% of dietary potassium can be secreted into the colon!**
  - **Intracellular Movement of Potassium** – Due to improved insulin sensitivity and natural alkali found in foods
  - **Bioavailability** (next slide)

Babich, John S., Kamyar Kalantar-Zadeh, and Shivam Joshi. "Taking the Kale out of Hyperkalemia: Plant Foods and Serum Potassium in Patients with Kidney Disease." *Journal of Renal Nutrition* (2022).

Bioavailability of Potassium in Plant Foods is Less than Animal Foods

- Cells of plants and animals differ
- Plants have cell walls; animals do not
- Plant cell walls are difficult to digest
  - Potassium is generally found inside cell-walls
- Potassium in plants is no more than 60% bioavailable in unprocessed fruits and vegetables

PRACTICAL ASPECTS

Potassium Additives and Bioavailability: Are We Missing Something in Hyperkalemia Management?

Check for updates

Kelly Picard, BSC, RD

Hyperkalemia and hyperphosphatemia are common metabolic disturbances in chronic kidney disease. Management may include instructions on a low-potassium or low-phosphorus diet, respectively. Low-phosphorus diet teaching includes information on phosphorus additives in addition to naturally occurring phosphorus food sources. Phosphorus additives are known to be more bioavailable compared with naturally occurring phosphorus. The concentration of phosphorus can also be much higher in processed foods compared with whole foods. Similar considerations may also be needed for dietary potassium teaching. The use of potassium additives

International Journal of Food Sciences and Nutrition, August 2008; 59(5): 438–450

informa healthcare

An investigation into the bioaccessibility of potassium in unprocessed fruits and vegetables

DONALD J. NAISMITH & ALESSANDRO BRASCHI

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Case Reports of Hyperkalemia with Plant-Based Foods

European Journal of Clinical Nutrition
https://doi.org/10.1038/s41430-018-0154-6

REVIEW ARTICLE

Review of case reports on hyperkalemia induced by dietary intake: not restricted to chronic kidney disease patients

Rogier P. M. te Dorsthorst[1] · Jytte Hendrikse[1] · Mats T. Vervoorn[1] · Valerie Y. H. van Weperen[1] · Marcel A. G. van der Heyden[2]

Received: 9 June 2017 / Revised: 19 February 2018 / Accepted: 28 February 2018

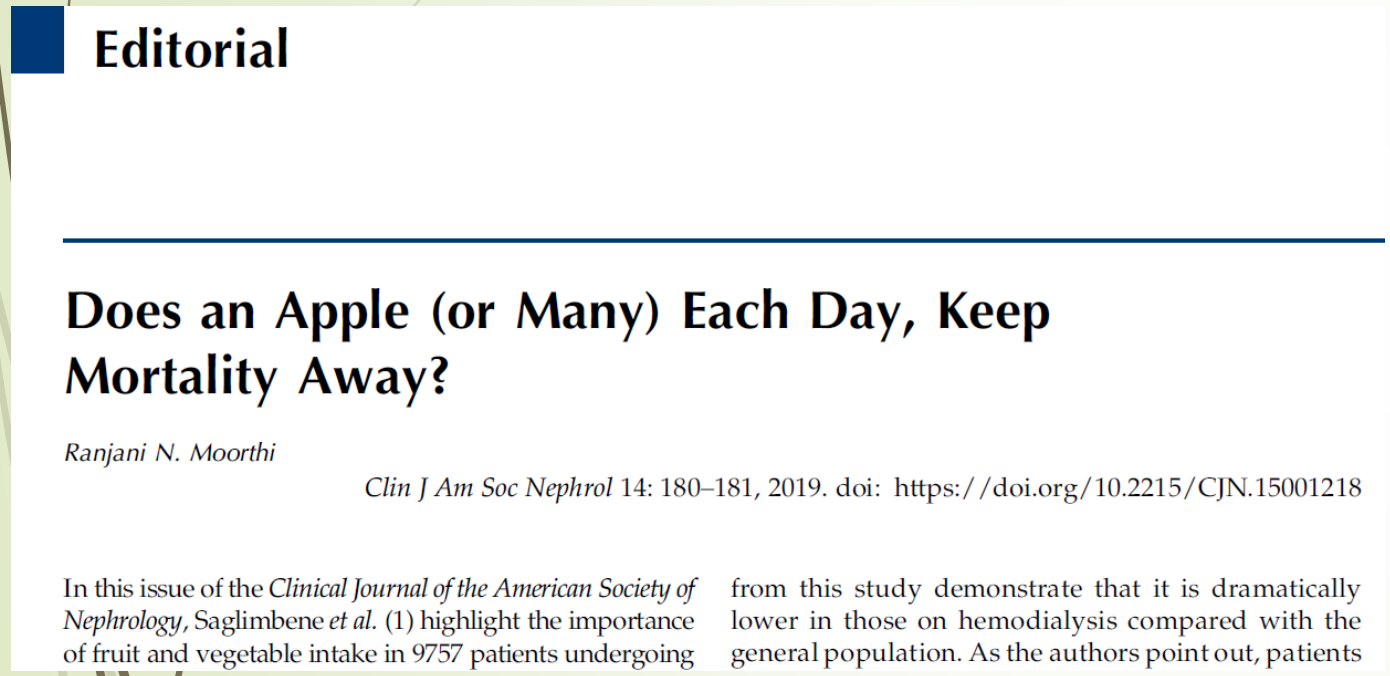
Abstract
Hyperkalemia is a metabolic disturbance of the potassium balance that can cause potentially fatal cardiac arrhythmias. Kidney dysfunction and renin–angiotensin–aldosterone system inhibiting drugs are notorious for their tendency to induce hyperkalemia by decreasing the excretion of potassium. The role of dietary potassium intake in inducing hyperkalemia is less clear. We review and analyze the common presentation, laboratory, and electrocardiogram (ECG) findings and therapeutic options associated with dietary-induced hyperkalemia, and find evidence for hyperkalemia development in non-renal

Most of the case reports are attributed to juices, sauces, and dried fruit – not unprocessed plant foods

Table 1 Overview of case reports of patients without underlying CKD/AKI (upper part) and with or non-specified CKD/AKI (lower part)

Author	Year	Origin of paper	Subjects	Cause	Age (sex)	CKD/AKI
Without underlying CKD/AKI						
Berk et al. [21]	2004	USA	1	Orange juice	66 (F)	No
Bosse et al. [22]	2011	USA	1	Potassium supplements	56 (F)	No
Briggs et al. [23]	2014	USA	1	Potassium supplements	44 (F)	No
Browning et al. [24]	1981	UK	1	Potassium citrate mix	83 (F)	No
Corbacioglu et al. [25]	2012	Turkey	1	Bananas	44 (F)	No
Epperly [26]	1987	USA	1	Baby food, fruit juices, and liquid supplements	80 (M)	No
Hoyt [27]	1986	USA	1	Salt substitute	70 (F)	No
Illingworth et al. [17]	1980	UK	1	40 slow potassium tablets	26 (M)	No
John et al. [28]	2011	Lebanon	2	Salt substitute, potassium supplements, sport nutritional drinks	65 (M); 35 (M)	Both: no
Kallen et al. [29]	1976	USA	1	Salt substitute	8 months (M)	No
Lisenbee et al. [30]	2012	USA	1	Potassium supplements	38 (M)	No
Pavletic [31]	2011	USA	1	Dried fruits	36 (F)	No
Restuccio [18]	1992	USA	1	Salt substitute	53 (M)	No
Rusyniak et al. [32]	2013	USA	1	Cream of tartar	16 (M)	No
Schim Van Der Loeff et al. [33]	1988	Netherlands	1	Salt substitute	29 (F)	No
Wetli et al. [19]	1978	USA	1	Potassium chloride	2 months (M)	No
With underlying CKD/AKI, or unknown/not specified						
Belknap [34]	1991	USA	1	Blackstrap molasses	67 (M)	Yes
Berrebi et al. [35]	2009	France	1	Fruit ingestion	57 (M)	Yes
Cheng et al. [36]	2005	Taiwan	1	Raw coconut juice	38 (M)	Yes
Corbacioglu et al. [25]	2012	Turkey	1	Apricot	58 (F)	Yes
Doorenbos et al. [37]	2003	Netherlands	1	Salt substitute	74 (F)	Yes
Fan et al. [38]	1996	USA	1	Orange juice	50 (M)	Yes
Gelfand et al. [39]	1975	USA	5	Geophagia	45 (M); 33 (M); 65 (F); 44 (F); 59 (F)	All: yes
Hakimian et al. [40]	2014	USA	1	Coconut water	42 (M)	Yes
Javed et al. [6]	2007	USA	1	Orange juice	51 (M)	Yes
Jones [41]	2004	USA	1	Tomato juice	68 (M)	Yes
Lamid et al. [42]	1978	USA	1	Tomato soup	62 (M)	Unknown
Leo et al. [43]	2011	Malaysia	1	Durian fruit	48 (F)	Yes
Mueller et al. [44]	2000	USA	1	Noni juice	?? (M)	Yes
Nagasaki et al. [8]	2005	Japan	1	Gerson therapy	52 (M)	Yes
Ray et al. [45]	1999	UK	2	Salt substitute and high potassium diet	67 (M); 64 (M)	Yes/Not specified
Rusyniak et al. [32]	2013	USA	1	Cream of tartar	32 (M)	Yes
Tazoe et al. [46]	2007	Japan	1	Bananas	15 (F)	Unknown
Wang [47]	1996	China	1	Bananas, peaches	23 (F)	Yes
Williams et al. [48]	2001	USA	1	Apple juice	70 (M)	Yes
Yap et al. [49]	1976	USA	2	Salt substitute	76 (M); 74 (M)	Both: Not specified
Yip et al. [50]	2012	China	1	Salt substitute	57 (F)	Yes

Got Hyperkalemia?



Editorial

Does an Apple (or Many) Each Day, Keep Mortality Away?

Ranjani N. Moorthi

Clin J Am Soc Nephrol 14: 180–181, 2019. doi: https://doi.org/10.2215/CJN.15001218

In this issue of the *Clinical Journal of the American Society of Nephrology*, Saglimbene *et al.* (1) highlight the importance of fruit and vegetable intake in 9757 patients undergoing

from this study demonstrate that it is dramatically lower in those on hemodialysis compared with the general population. As the authors point out, patients

The inadvertent consequence of this avoidance is that they fail to derive benefits from fruits and vegetables such as the antioxidants, fiber, and other benefits. Despite this recommendation, there is actually little data to support that eating fruits and vegetables increases serum potassium.

Summary of Evidence Showing Nearly No Increase in Potassium with Plant-Based Diets

Name	Quantity of Plants Consumed	Size	Duration/Type	Increase in Potassium?	Stage of CKD	Comment
Goraya Kidney Int 2012	Typically 2 to 4 cups	199	30 days Controlled trial	No	I/II	
Goraya Kidney Int 2014	2 to 4 cups	108	3 years RCT	No	III	
Tyson CKJ 2016	DASH diet	10	2 weeks Controlled trial	No	III	
Moorthi AJN 2014	70% plant protein	13	4 weeks Controlled trial	No but	III/IV	1 patient with type IV RTA
Barsotti Nephron 1996	Vegetarian diet	37	3 months Controlled trial	No	III-V	14 months data on K not reported
Goraya CJASN 2013	2 to 4 cups	76	1 year RCT	No	IV	
Wu Nephrology 2011	Vegetarian diet	19	Cross-sectional	No	HD	
St-Jules J Ren Nutr 2016	Increasing K+ intake	140	Cross-sectional	No	HD	No correlation b/w serum K+ & dietary K
Saglimbene JASN 2019	Median 8 servings F+V/week	8078	Prospective observational (median 2.8 years)	No	HD	
Gonzalez Ortiz NDT 2020	Plant-based diet score	150	Prospective (1 year)	No	HD	

Babich, John S., Kamyar Kalantar-Zadeh, and Shivam Joshi. "Taking the Kale out of Hyperkalemia: Plant Foods and Serum Potassium in Patients with Kidney Disease." *Journal of Renal Nutrition* (2022).

The One Patient with Hyperkalemia (with a known Type IV RTA)

"There were a total of 2 incidences of potassium of 5.8 mEq/l and both these measures were in the same subject, with a known type IV RTA, which required modifying the plant protein source from raw edamame (482 mg of potassium/100 g) the highest potassium content among all plant sources (National Database for Standard Reference: USDA Release 26) to fried tofu."[1]

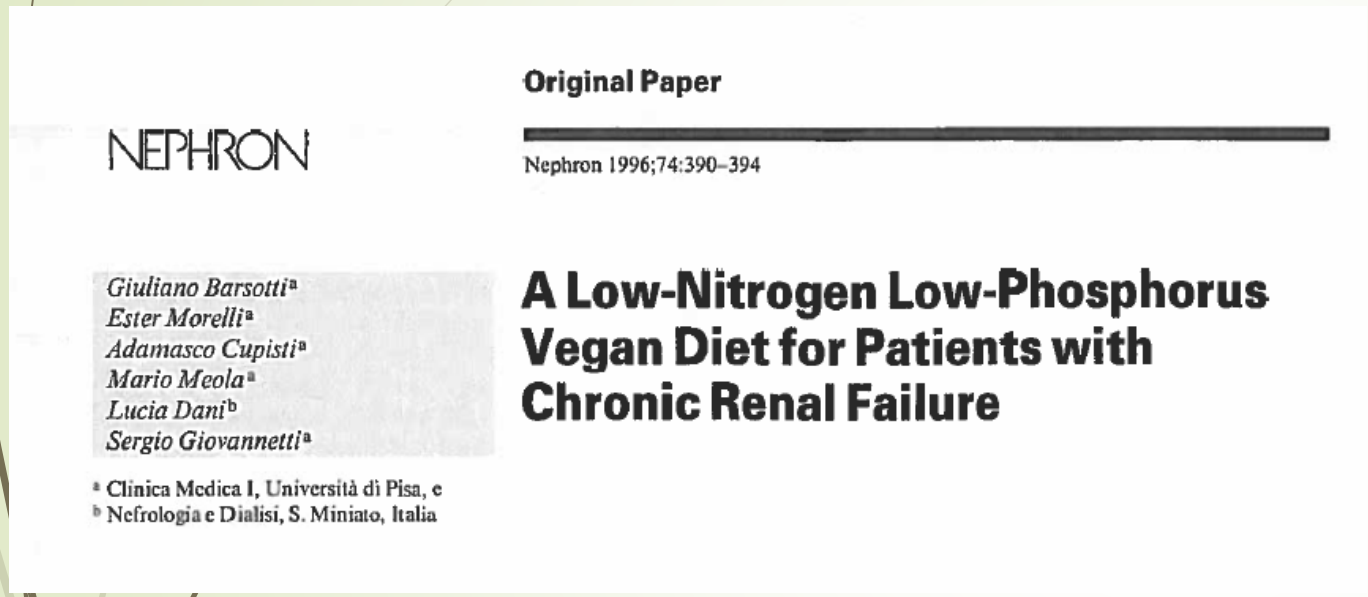
[1]Moorthi, Ranjani N. *American Journal of Nephrology* 40.6 (2014): 582-591.

Foods with the Most Potassium

NDB_No	Description	Weight(g)	Measure	Potassium, K (mg) Per Measure
19304	Molasses	337.0	1.0 cup	4934
11432	Radishes, oriental, dried	116.0	1.0 cup	4053
11382	Potatoes, mashed, dehydrated, granules with milk, dry form	200.0	1.0 cup	3696
16049	Beans, white, mature seeds, raw	202.0	1.0 cup	3626
16108	Soybeans, mature seeds, raw	186.0	1.0 cup	3342
16045	Beans, small white, mature seeds, raw	215.0	1.0 cup	3315
19355	Syrups, sorghum	330.0	1.0 cup	3300
12005	Seeds, breadnut tree seeds, dried	160.0	1.0 cup	3218
16040	Beans, pink, mature seeds, raw	210.0	1.0 cup	3074
16071	Lima beans, large, mature seeds, raw	178.0	1.0 cup	3069
16119	Soy meal, defatted, raw	122.0	1.0 cup	3038
01115	Whey, sweet, dried	145.0	1.0 cup	3016
16014	Beans, black, mature seeds, raw	194.0	1.0 cup	2877

USDA Food Composition Database. https://ndb.nal.usda.gov/ndb/search/list?home=true. Accessed 5/8/19.

Got Hyperkalemia?



NEPHRON

Original Paper

Nephron 1996;74:390–394

Giuliano Barsotti[a]
Ester Morelli[a]
Adamasco Cupisti[a]
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[a] Clinica Medica I, Università di Pisa, e
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A Low-Nitrogen Low-Phosphorus Vegan Diet for Patients with Chronic Renal Failure

Table 4. Serum and urine biochemical parameters in patients with severe chronic renal failure on the SVD, CLPD or UPD, for at least 3 months

	SVD	CLPD	UPD
n	15	15	10
CRcl, ml/min	15.6±7.5	14.2±4.6	14.6±4.6
sUrea, mg/dl	73±34***	83±29***	132±33
uUrea, g/24 h	8.1±2.8***	8.3±2.3***	13.5±2.3
sP_i, mg/dl	3.8±0.7	4.0±1.0	4.4±1.2
uP_i, mg/24 h	457±121*	405±86**	561±114
sCa, mg/dl	9.0±0.8	8.6±0.7	8.6±1.2
sK^+, mEq/l	4.5±0.7	4.4±0.5	4.6±0.8
Capillary pH	7.36±0.04	7.37±0.04	7.34±0.06
HCO_3^-, mmol/l	20.3±2.9*	20.2±2.4*	17.6±3.4
Urinary pH	6.49±0.58**	5.99±0.86	5.50±0.47
TA, mmol/24 h	5.7±3.7***	9.1±5.0**	16.7±6.2
NH_4, mmol/24 h	3.4±1.4*	5.7±2.8	6.7±2.5
Total H^+, mmol/24 h	9.1±5.3**	14.8±7.1**	23.4±6.6

TA = Titratable acid.
*** $p<0.001$, ** $p<0.01$, * $p<0.05$, vs. UPD.

- Data on 22 patients with CKD III to V (eGFR 15) on a vegan diet for 3 months (14 month data not reported)

Recent Review Article

ARTICLE IN PRESS

REVIEW ARTICLE

Taking the Kale out of Hyperkalemia: Plant Foods and Serum Potassium in Patients With Kidney Disease

John S. Babich, BS, Kamyar Kalantar-Zadeh, MD, MPH, PhD,† and Shivam Joshi, MD‡,§*

Traditionally, diets for kidney disease were low in potassium. This recommendation was based on outdated research and often wrong assumptions that do not reflect current evidence. In fact, studies conducted over the past decades show patients with CKD, including kidney failure, do not benefit from the restriction of plant foods relative to control. Generally, dietary potassium does not correlate with serum potassium, and we posit that this is due to the effects of fiber on colonic potassium absorption, the alkalinizing effect of fruits and vegetables on metabolic acidosis, and the bioavailability of dietary potassium in plant foods. Also, consumption of plant foods may provide pleiotropic benefits to patients with CKD. Emerging dietary recommendations for kidney health should be devoid of dietary potassium restrictions from plant foods so that patient-centered kidney recipes can be encouraged and promoted.

Keywords: potassium; renal insufficiency; diet; vegan; metabolic acidosis; nutrition policy

Dietary Protein Adequacy

Do patients with CKD get enough protein on a plant-based diet?

- Example 1
  - 1996 Italian study placed 37 patients with stage III/IV CKD on a low-protein (0.7 g/kg/day), "special vegan diet" comprised of a prespecified combination of cereals and legumes (based on the now-discarded idea of protein complementation)
    - A subset (twenty-two) of the patients were followed for a mean of 13 months and did not show any signs of nutritional deficiency, while on an exclusively plant-based diet

Barsotti G, Morelli E, Cupisti A, Meola M, Dani L, Giovannetti S. A low-nitrogen low-phosphorus Vegan diet for patients with chronic renal failure. *Nephron*. 1996;74(2):390-394.

- Example 2
  - 15 Israeli patient with stage III/IV patients on a near-total plant-based diet consuming 0.75 g/kg/day of protein for six months did not show any nutritional deficits
  - *Those consuming a plant-based diet actually had better dietary compliance and caloric intakes than their animal-protein diet counterparts*
    - Less inflammation and uremic toxin development (?)

Soroka N, Silverberg DS, Greemland M, et al. Comparison of a vegetable-based (soya) and an animal-based low-protein diet in predialysis chronic renal failure patients. *Nephron*. 1998;79(2):173-180.

Do patients on hemodialysis get enough protein on a plant-based diet?

- HD patients recommended to get **1.0-1.2 g/kg/day**
- Two studies of vegetarians on hemodialysis showed protein intake of **1.2-1.25 g/kg/day** without compromise[1,2]
- Unclear from studies if their diets were modified in any way (versus eating ad lib) or supplemented with protein-containing foods

[1]Wu T, Chang C, Hsu W, et al. Nutritional status of vegetarians on maintenance haemodialysis. *Nephrology*. 2011;16(6):582-587.

[2]Kandouz S, Mohamed AS, Zheng Y, Sandeman S, Davenport A. Reduced protein bound uraemic toxins in vegetarian kidney failure patients treated by haemodiafiltration. *Hemodialysis International*. 2016;20(4):610-617.

NEPHROLOGY

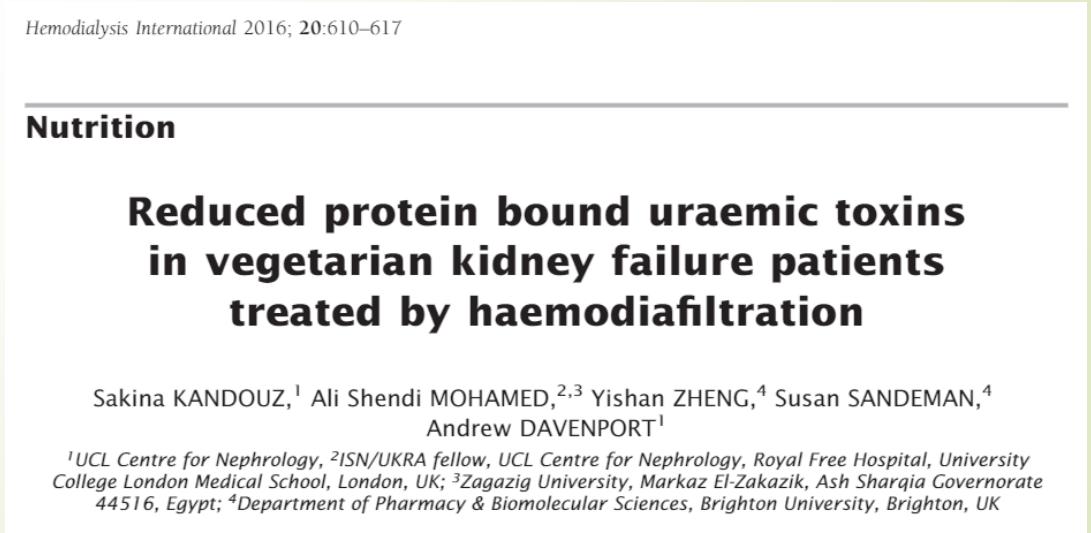
Nephrology **16** (2011) 582–587

Original Article

Nutritional status of vegetarians on maintenance haemodialysis

TAI-TE WU,[1]* CHIEH-YING CHANG,[1]* WEI-MIN HSU,[2] I-KWAN WANG,[3] CHIH-HAO HSU,[1] SHU-HWA CHENG,[1] CHIH-CHIA LIANG,[3] CHIZ-TZUNG CHANG[3] and CHIU-CHING HUANG[3]

[1]Chun-An Dialysis Centre, Taoyuan, [2]Zen-Ho Dialysis Centre and [3]Division of Nephrology, China Medical University Hospital and College of Medicine, Taichung, Taiwan



Hemodialysis International 2016; **20**:610–617

Nutrition

Reduced protein bound uraemic toxins in vegetarian kidney failure patients treated by haemodiafiltration

Sakina KANDOUZ,[1] Ali Shendi MOHAMED,[2,3] Yishan ZHENG,[4] Susan SANDEMAN,[4] Andrew DAVENPORT[1]

[1]UCL Centre for Nephrology, [2]ISN/UKRA fellow, UCL Centre for Nephrology, Royal Free Hospital, University College London Medical School, London, UK; [3]Zagazig University, Markaz El-Zakazik, Ash Sharqia Governorate 44516, Egypt; [4]Department of Pharmacy & Biomolecular Sciences, Brighton University, Brighton, UK

A Variety of Plant-Foods Provide Adequate Protein with Typical Consumption

PRACTICAL ASPECTS

Adequacy of Plant-Based Proteins in Chronic Kidney Disease

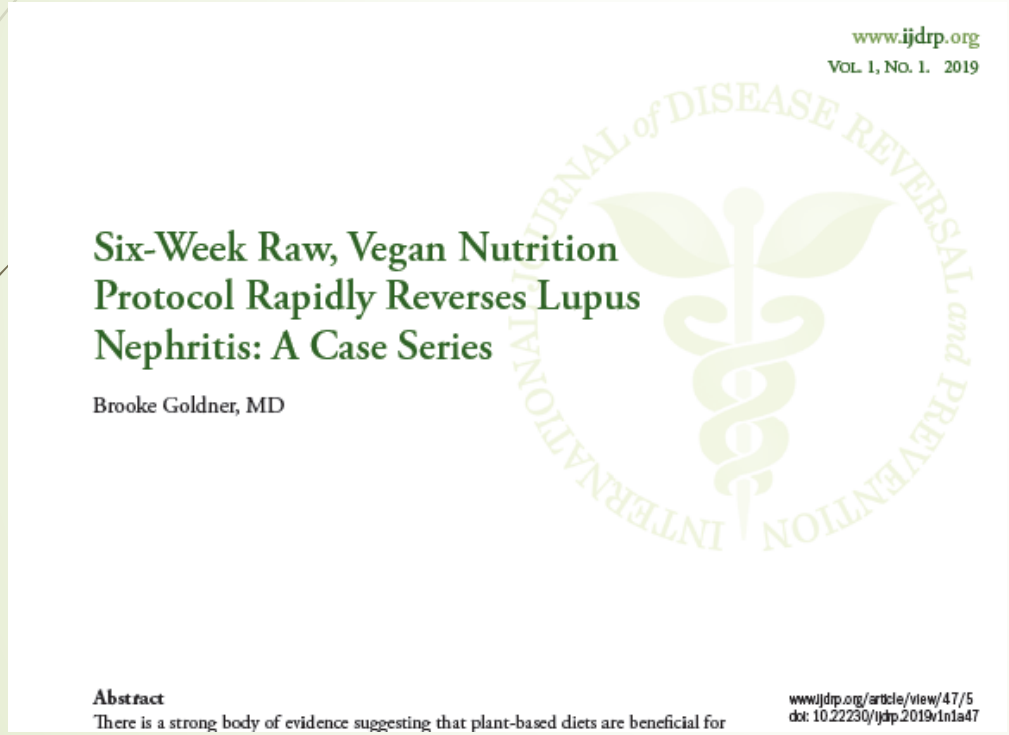
Shivam Joshi, MD, Sanjeev Shah, MD,* and Kamyar Kalantar-Zadeh, MD†*

Concerns regarding protein and amino acid deficiencies with plant-based proteins have precluded their use in chronic kidney disease (CKD) patients. Many of these concerns were debunked years ago, but recommendations persist regarding the use of "high-biological value" (animal-based) proteins in CKD patients, which may contribute to worsening of other parameters such as blood pressure, metabolic acidosis, and hyperphosphatemia. Plant-based proteins are sufficient in meeting both quantity and quality requirements. Those eating primarily plant-based diets have been observed to consume approximately 1.0 g/kg/day of protein, or more. CKD patients have been seen to consume 0.7-0.9 g/kg/day of mostly plant-based protein without any negative effects. Furthermore, those substituting animal-based proteins for plant-based proteins have shown reductions in severity of hypertension, hyperphosphatemia, and meta-

It is important to note that amino acid deficiency is possible in those who are eating a restrictive diet limited to one or two food sources, creating a situation such that attaining the RDA for an amino acid may exceed the number of servings than is humanly possible. A stark example of this can be illustrated by the low tryptophan content of an apple. A medium-sized (100 g) apple contains 1 mg of tryptophan.[18] Based on the RDA for tryptophan (5 mg/kg/day), a 70-kg person would need on average 350 mg of tryptophan per day.[4] To meet this, a person eating a diet exclusively of apples would need to eat 350 apples daily to meet the RDA for tryptophan, which is not possible in a real-world scenario.

Reversing Disease

Treating/Reversing Lupus Nephritis?



www.ijdrp.org
VOL. 1, NO. 1. 2019

Six-Week Raw, Vegan Nutrition Protocol Rapidly Reverses Lupus Nephritis: A Case Series

Brooke Goldner, MD

Abstract
There is a strong body of evidence suggesting that plant-based diets are beneficial for

www.ijdrp.org/article/view/47/5
doi: 10.22230/ijdrp.2019v1n1a47

- Anecdotal but hypothesis-generating
- 2 cases of patients with lupus nephritis having improvement in GFR after consuming six-weeks of a raw, vegan diet
- Case 1: GFR 14 -> 27
- Case 2: GFR 53 -> 73

Treating/Reversing Minimal Change Disease?

PatientVoice

Diet and Risk for Developing Kidney Disease

Duane Sunwold

Clin J Am Soc Nephrol 14: 1–2, 2019. doi: https://doi.org/10.2215/CJN.13601118

I was diagnosed with minimal changes disease, and I am very interested in research that shows lifestyle patterns that affect kidney disease. I was diagnosed 18 years ago and have spent the past two decades successfully experimenting with food and how protein affects my kidney disease. By replacing animal protein with plant-based protein, I was able to put my CKD into remission.

In this issue of the *Clinical Journal of the American Society of Nephrology*, Rebholz *et al.* (1) research the effect of sugar-sweetened beverages on kidney disease risk. Important studies, such as this one, motivate me

1. I educate patients. I remind them to read nutritional labels and record the amount of sugar that they consume in a day from beverages. I had to learn how addictive sugar is for me; the more I consume, the more I crave it. If I start drinking a soda with lunch, I will start craving a soda at every lunch.
2. I explain to patients that eating is a journey with kidney disease. How can I make this journey as enjoyable and healthy as possible? People look at food and beverage as a one-time event, a meal that we sit down and enjoy. As a patient, I had to

Inland Northwest Culinary Academy, Spokane Community College, Spokane, Washington

Correspondence: Duane Sunwold, Instructor, Inland Northwest Culinary Academy, Spokane Community College, Spokane, WA 99217

Treating/Reversing Minimal Change Disease?

Can Comprehensive Lifestyle Change Alter the Course of Chronic Kidney Disease?

Katherine R. Tuttle, MD,*† Duane Sunwold,‡ and Holly Kramer, MD, MPH§,‖

Summary: Comprehensive lifestyle change can impact health favorably in many domains, from prevention and treatment of various diseases to improved functional status and quality of life. Although habitual behaviors clearly influence chronic kidney disease (CKD), lifestyle change often is not stressed in the clinical setting. The purpose of this review is to provide a critical appraisal of the scientific basis for effects of lifestyle on CKD and practical strategies that promote healthy behaviors. This review begins with a clinical case presentation to provide context for the scientific discussion. Dietary composition of macronutrients, particularly protein intake, is highlighted. Clinical evidence is presented for avoiding protein excess, a contemporary problem in the typical overeating environment of the developed world. Concomitant approaches to balancing intake of carbohydrates and fats also are presented. Integration of sodium reduction with macronutrient adjustment is reviewed within the framework of managing blood pressure in the setting of CKD. Considering the emerging body of evidence for obesity-related CKD and associated complications, weight control is addressed from the standpoint of decreasing calories and increasing exercise. Finally, effects of smoking and alcohol use on CKD are discussed. In the spirit of active participation, which is essential to lifestyle change, the discussion returns full circle to a concluding statement from the clinical case patient who provides his point of view on lifestyle change while living with CKD.

Semin Nephrol 29:512-523

Keywords: *Dietary protein, macronutrients, sodium, obesity, exercise*

- 44 year old gentleman w/ obesity (BMI 38 kg/m^2), uncontrolled hypertension, nephrotic range proteinuria (13g/day) and a creatinine of 2.0 mg/dL
- Biopsy: minimal change disease
- Unresponsive to prednisone 60 mg/d and cyclosporine -> Creatinine worsened to 4.2 mg/dL
- Prednisone 60 mg/day + Mycophenolate mofetil reduced creatine to 2.6 mg/dL and proteinuria to 4.0 g/day
- Adopted a whole-foods plant-based (vegan) diet + swimming -> Lost 60 lbs (BMI fell to 24 kg/m^2), creatinine improved to 1.2 mg/dL, urine albumin level 12 mg/g
- Regained his life

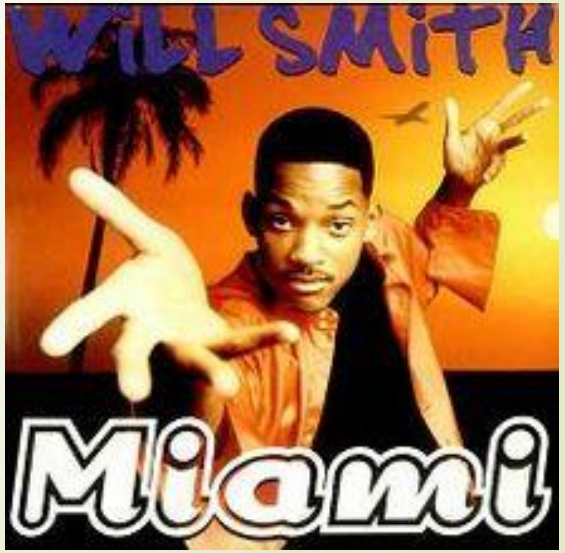
In His Own Words

I appreciate the recommendations my doctor gave me about making dietary modifications: replace your protein intake with plant-based protein. This one change has had a monumental impact on my life. I have gained back a quality of life that I thought was gone forever. My benchmark for normal has been my ability to keep up with my professional work demands and still be able to exercise. For the past 7 months, I now swim 5,000 meters every other day; a distance that surpasses my pre-kidney disease life. I perceived I lived a healthy lifestyle before kidney disease; today I live a healthier, happier lifestyle and I have my kidneys to thank for it.

Big Picture & Conclusion

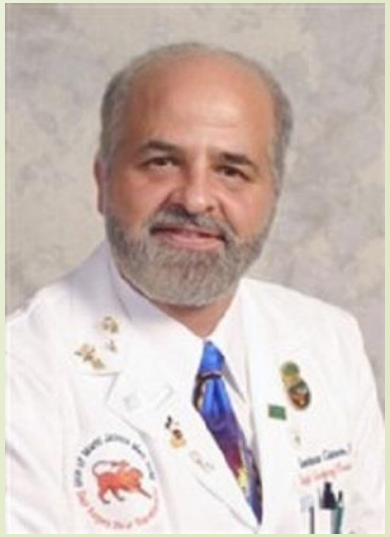
Rewind to 2008

- I had just started medical school at the University of Miami…
- I had no idea what kind of doctor I wanted to become…
- I listened to “Welcome to Miami” on loop…

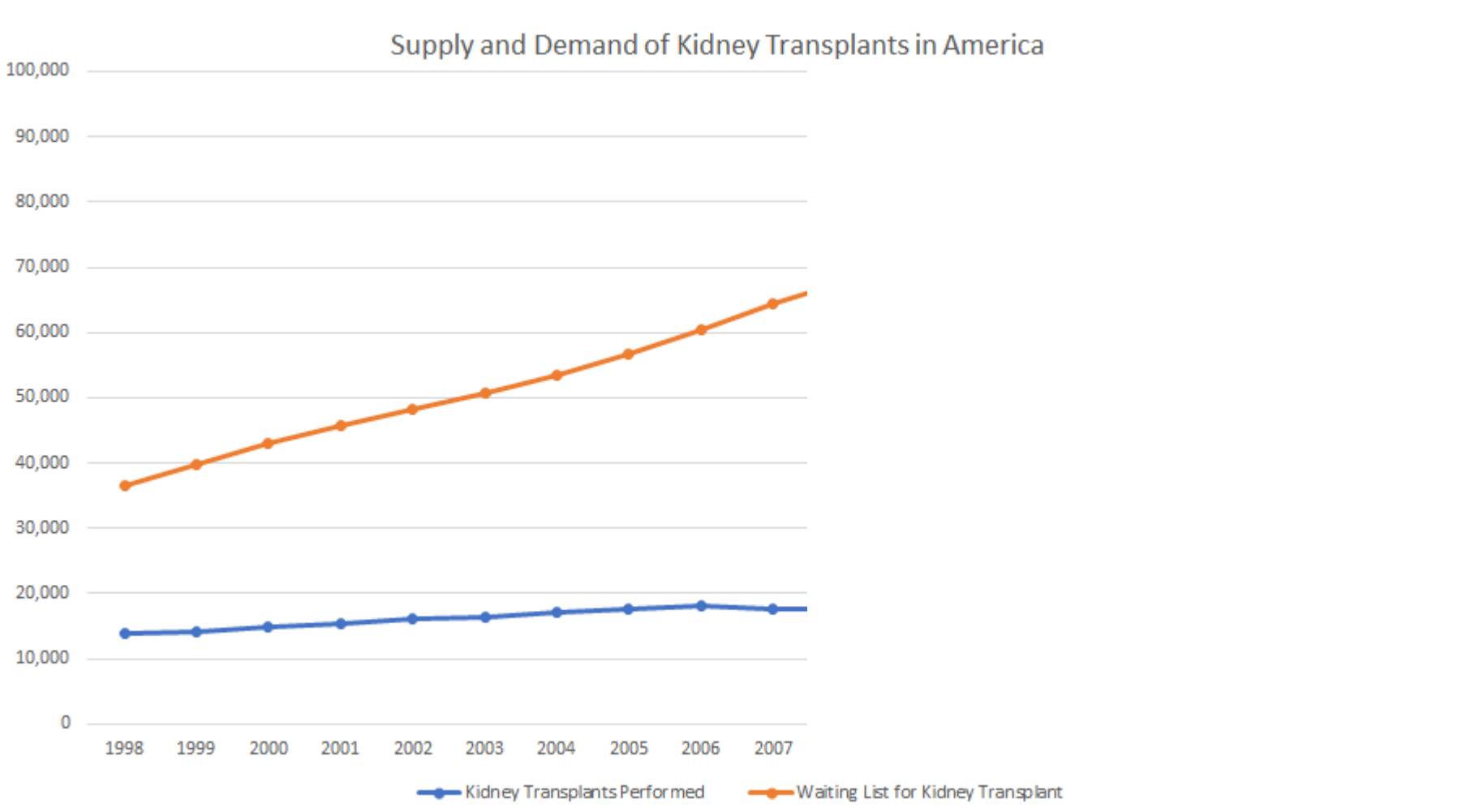


Still in 2008…

- I became incredibly interested in kidney transplantation…
- And so I started to do research in the field of kidney transplantation

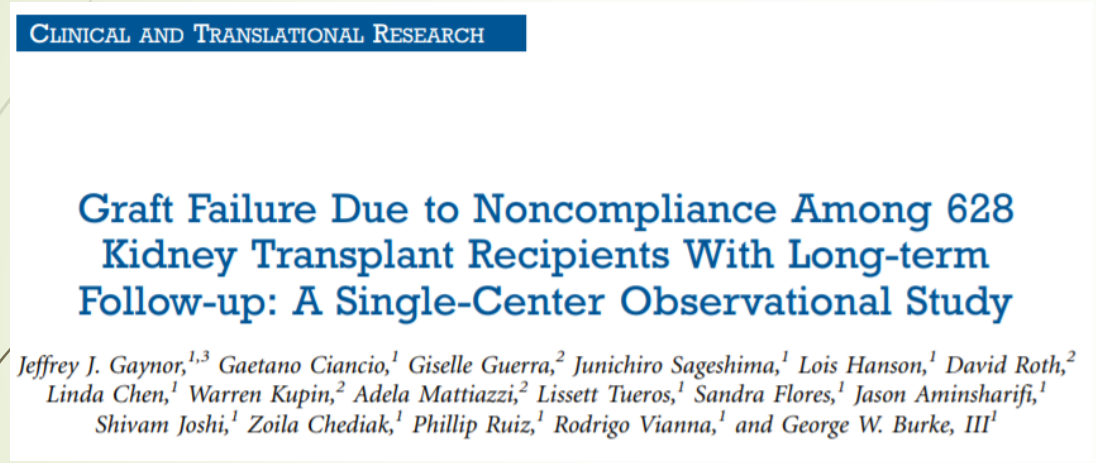


Supply and Demand of Kidney Transplants



Source: USRDS; www.usrds.org

2008 – 2012: My research into these issues….



CLINICAL AND TRANSLATIONAL RESEARCH

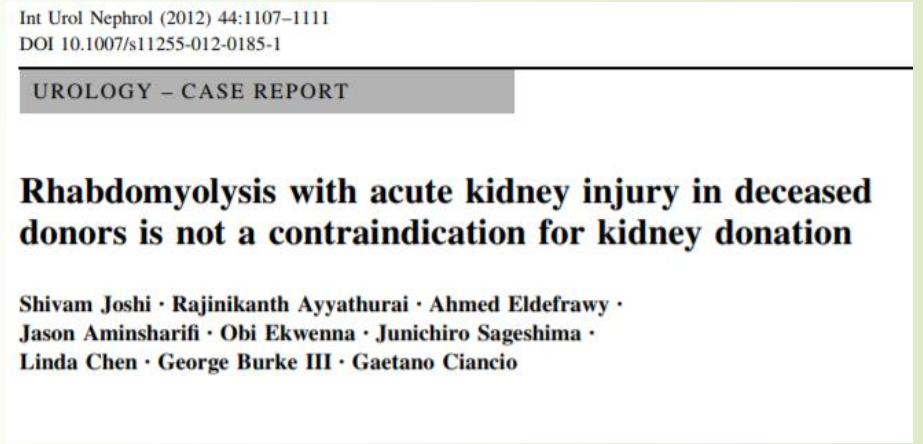
Graft Failure Due to Noncompliance Among 628 Kidney Transplant Recipients With Long-term Follow-up: A Single-Center Observational Study

Jeffrey J. Gaynor,[1,3] Gaetano Ciancio,[1] Giselle Guerra,[2] Junichiro Sageshima,[1] Lois Hanson,[1] David Roth,[2] Linda Chen,[1] Warren Kupin,[2] Adela Mattiazzi,[2] Lissett Tueros,[1] Sandra Flores,[1] Jason Aminsharifi,[1] Shivam Joshi,[1] Zoila Chediak,[1] Phillip Ruiz,[1] Rodrigo Vianna,[1] and George W. Burke, III[1]

CLINICAL AND TRANSLATIONAL RESEARCH

Disparities Among Blacks, Hispanics, and Whites in Time From Starting Dialysis to Kidney Transplant Waitlisting

Shivam Joshi,[1] Jeffrey J. Gaynor,[1] Stephanie Bayers,[1] Giselle Guerra,[2] Ahmed Eldefrawy,[3] Zoila Chediak,[1] Lazara Companioni,[1] Junichiro Sageshima,[1] Linda Chen,[1] Warren Kupin,[2] David Roth,[2] Adela Mattiazzi,[2] George W. Burke, III,[1] and Gaetano Ciancio[1,3,4,5]

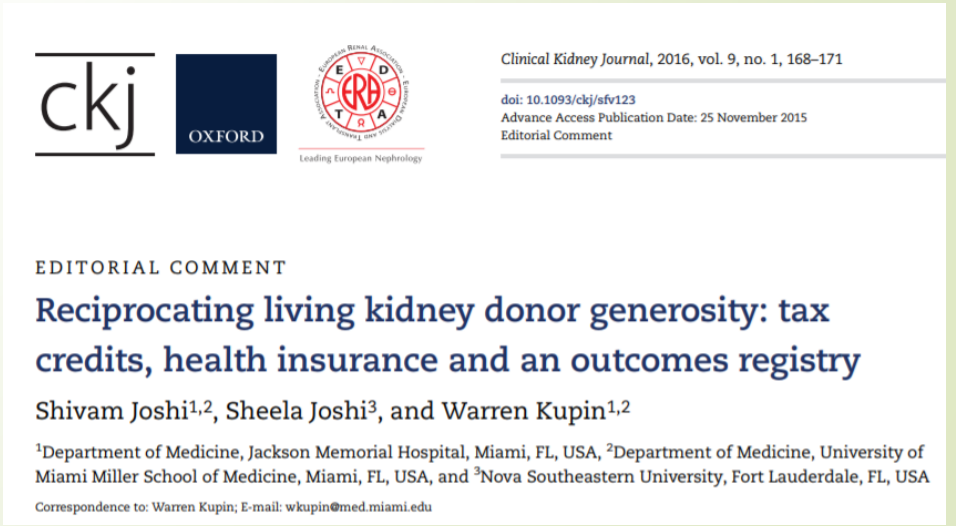


Int Urol Nephrol (2012) 44:1107–1111
DOI 10.1007/s11255-012-0185-1

UROLOGY – CASE REPORT

Rhabdomyolysis with acute kidney injury in deceased donors is not a contraindication for kidney donation

Shivam Joshi · Rajinikanth Ayyathurai · Ahmed Eldefrawy · Jason Aminsharifi · Obi Ekwenna · Junichiro Sageshima · Linda Chen · George Burke III · Gaetano Ciancio



ckj OXFORD

Clinical Kidney Journal, 2016, vol. 9, no. 1, 168–171

doi: 10.1093/ckj/sfv123
Advance Access Publication Date: 25 November 2015
Editorial Comment

EDITORIAL COMMENT

Reciprocating living kidney donor generosity: tax credits, health insurance and an outcomes registry

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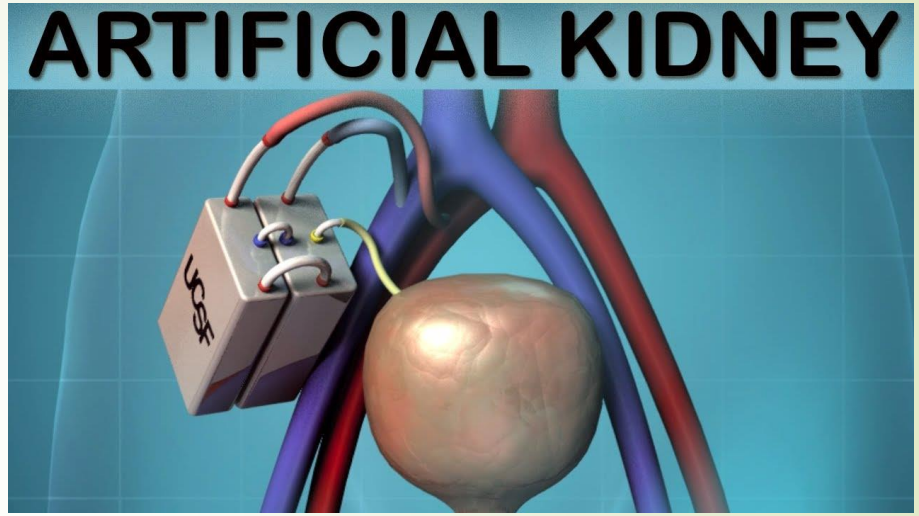
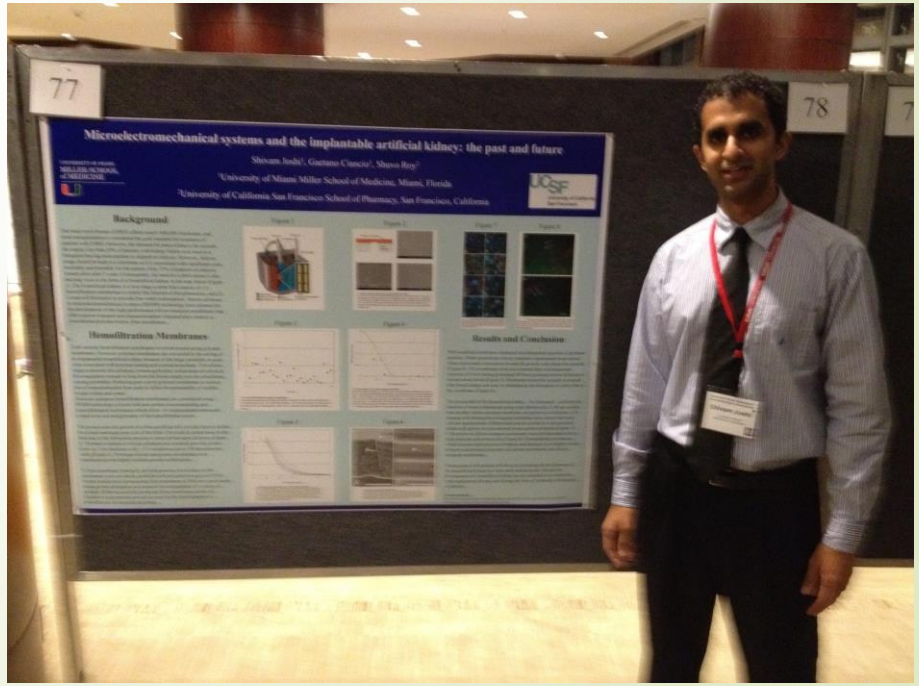
Summer of 2012

- I graduated medical school
- I deferred residency and went to work on artificial kidneys

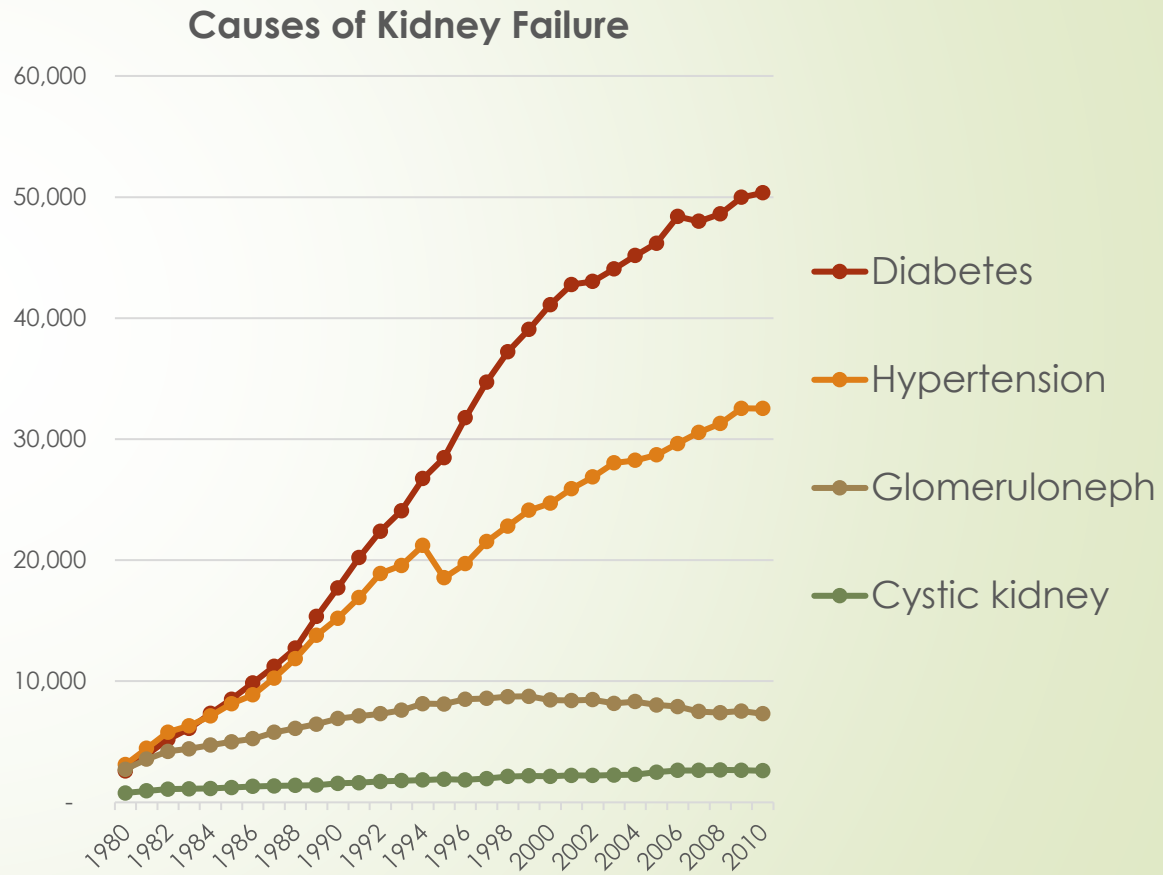




2012 - 2013

I learned a couple things:

- Making an artificial kidney is **incredibly hard, if not impossible**
  - May not happen in our lifetimes unfortunately
- The main causes of kidney failure… **are diabetes and high blood pressure**



Source: USRDS; www.usrds.org

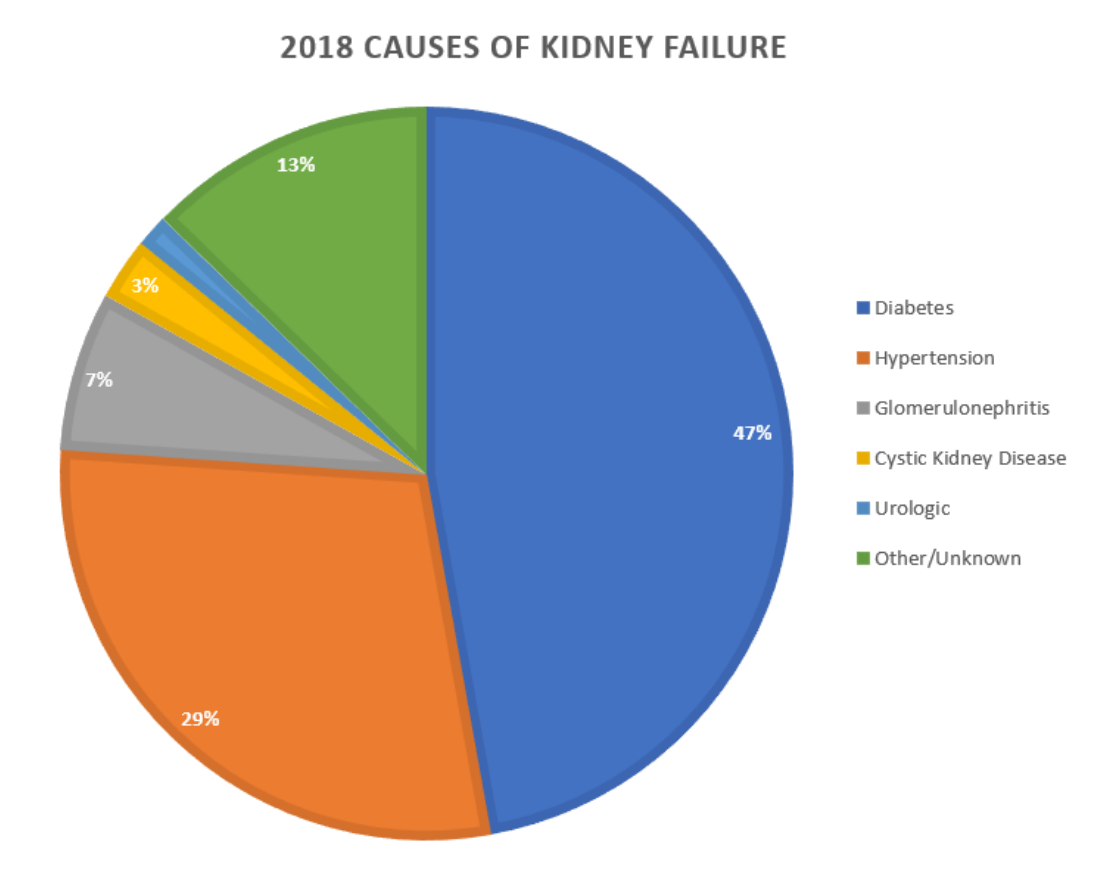
And then the light bulb went off…

Type 2 diabetes and hypertension need not happen.

Type 2 diabetes and hypertension need not be uncontrolled.

Type 2 diabetes and hypertension need not cause kidney failure.

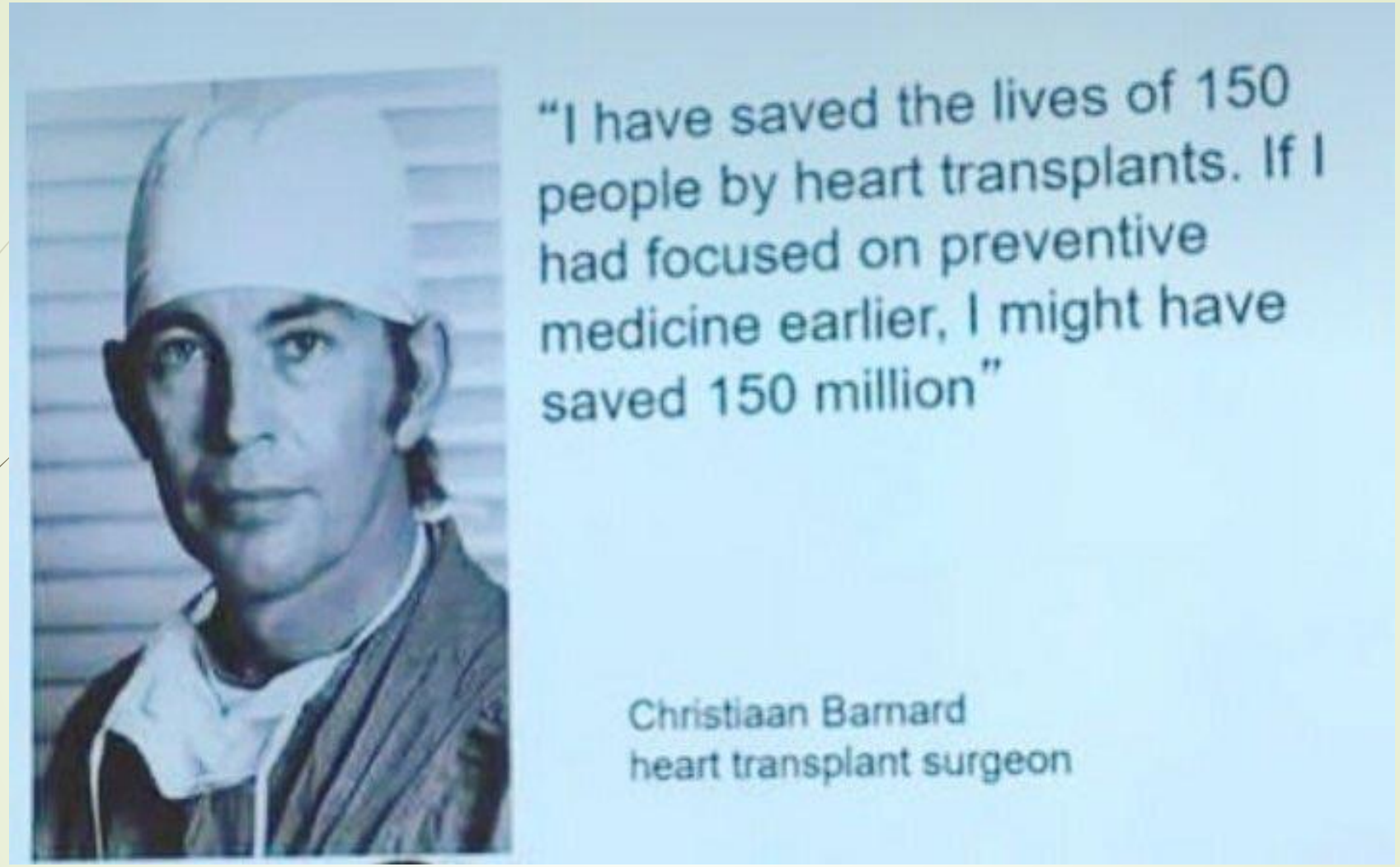
78% of Kidney Failure: Diabetes and High Blood Pressure



United States Renal Data System. 2018 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2018.

- **Diabetes**
  - 90% of all diabetes is type 2 diabetes[1]
  - 90% of type 2 diabetes is preventable[2]
- **High Blood Pressure**
  - 80% of high blood pressure is preventable

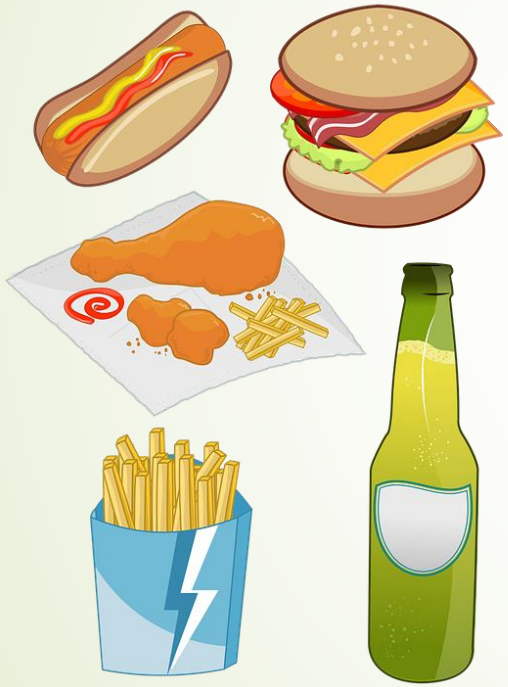
[1] https://www.cdc.gov/diabetes/basics/type2.html
[2] Hu, Frank B., et al. "Diet, lifestyle, and the risk of type 2 diabetes mellitus in women." *New England journal of medicine* 345.11 (2001): 790-797.
[3] Forman, John P., Meir J. Stampfer, and Gary C. Curhan. "Diet and lifestyle risk factors associated with incident hypertension in women." *Jama* 302.4 (2009): 401-411.



Christiaan Barnard, MD, performed the first human heart transplant

https://twitter.com/KoushikReddyMD/status/1089886531324702720

“An ounce of prevention…”



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- Type 2 diabetes
- Prediabetes
- High blood pressure
- High cholesterol
- Excess weight
- Heart disease

Dr. Michelle McMacken, director of the NYC Health + Hospitals/Bellevue's Plant-Based Lifestyle Medicine Program

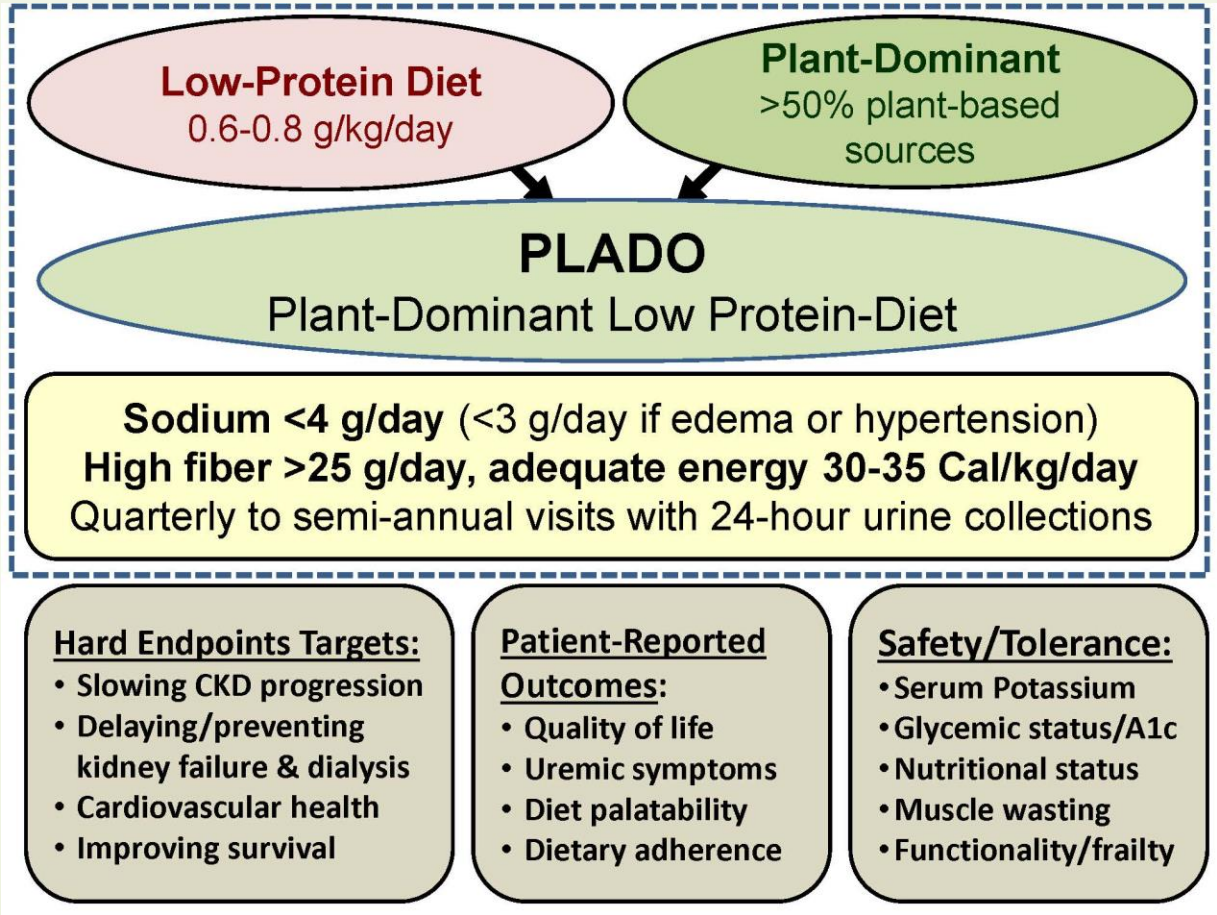
In Summary: Role of Plant-Based Diets in CKD Management

Preventing the Causes of Kidney Disease:
Type 2 Diabetes
Hypertension
Obesity

Attenuating the Progression of Kidney Disease:
eGFR decline
Albuminuria

Reducing the Complications of Kidney Disease:
Hyperphosphatemia
Metabolic Acidosis
Renal Hypertension
Uremic Toxins
Mortality

Plant-Dominant Low-Protein (PLADO) Diet for Chronic Kidney Disease

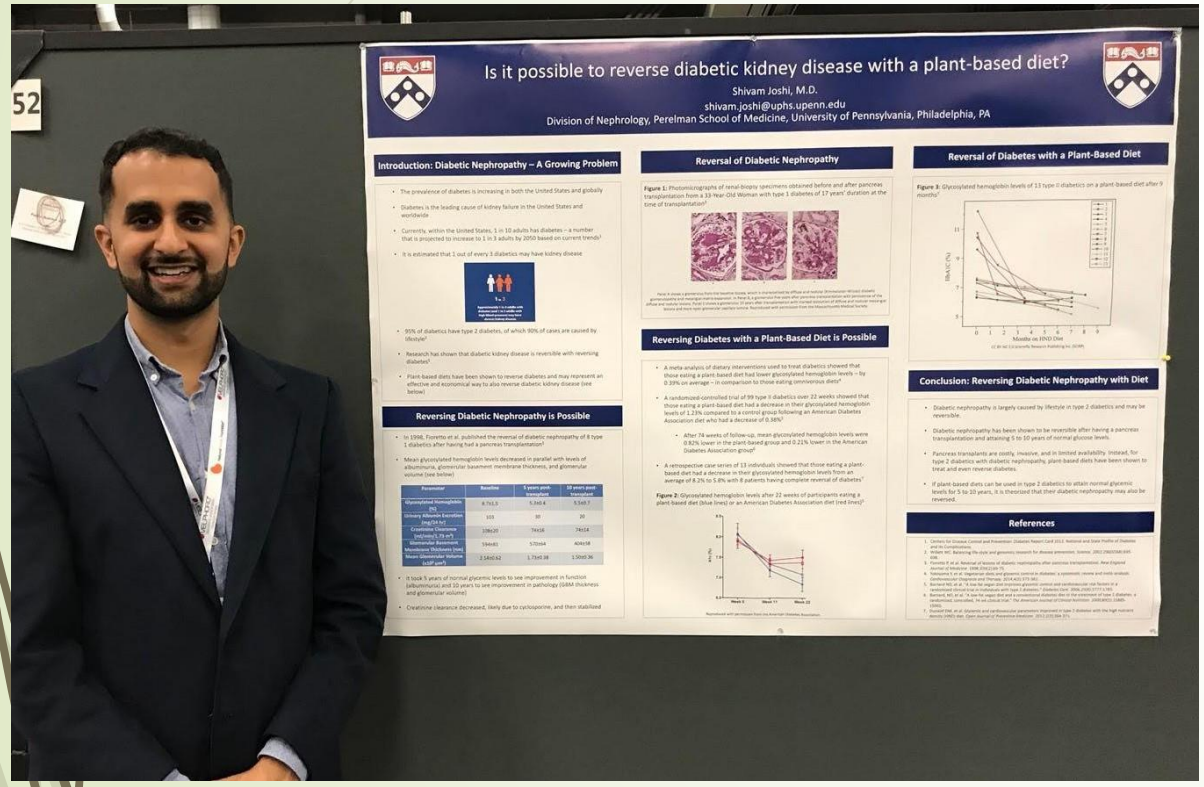


Kalantar-Zadeh, Kamyar, et al. "Plant-dominant low-protein diet for conservative management of chronic kidney disease." *Nutrients* 12.7 (2020): 1931.

Acknowledgements

- Dr. Katherine Tuttle (University of Washington)
- Dr. Kam Kalantar-Zadeh (UC Irvine)
- Dr. Joel Kopple (UCLA)
- Dr. Raymond Townsend (Penn)
- Dr. Sid Shah (Penn)
- Dr. Sanjeev Shah (Penn)
- Dr. Neal Barnard (George Washington)
- Dr. Michelle McMacken (NYU)
- Dr. David St-Jules (University of Nevada, Reno)
- Dr. David Goldfarb (NYU)
- Lauren Graf
- National Kidney Foundation

Thank You!



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Questions?